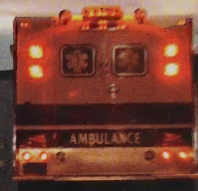


Harvard Medicine

SPRING 2017



Is rural health care
out of reach?

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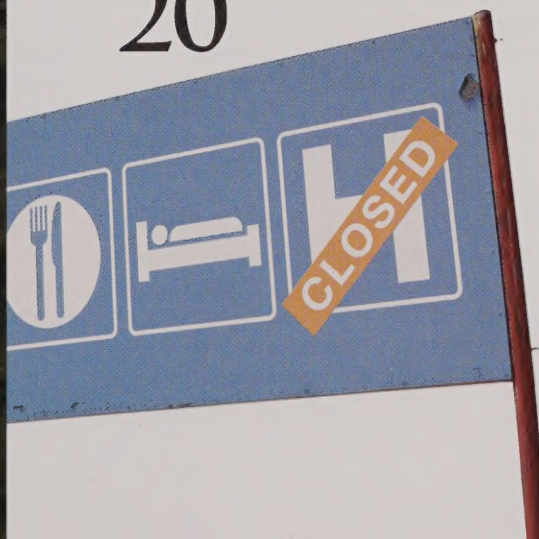
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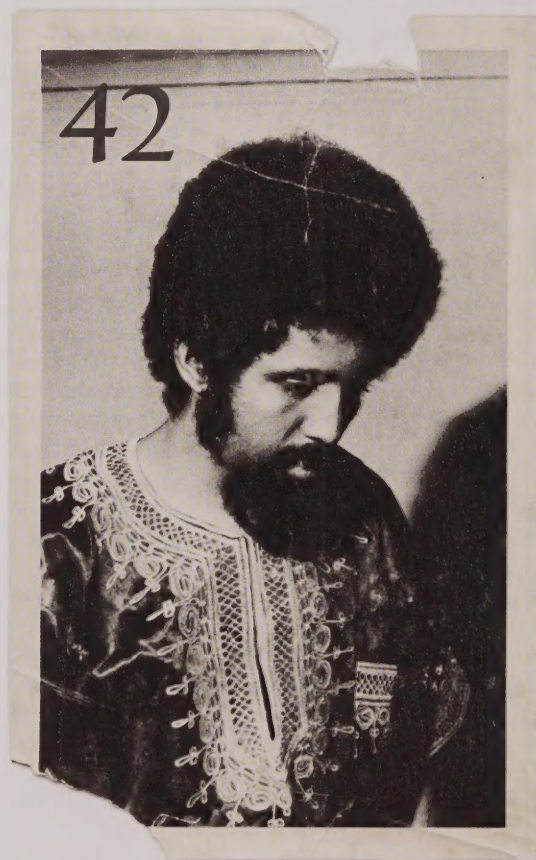
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From the Dean



MY GRANDFATHER AND I share more than a last name, we share a profession. He was the village physician in Athens, New York. In that role, he attended to every sort of medical condition his neighbors faced—and in any weather the Upper Hudson Valley could produce. He was an integral part of his community, a personification of the shared spirit that held people together.

Rural doctors still foster that sense of community, still fill that need for an anchor in hard times. The general practitioner of my grandfather's era has specialized, becoming the primary care or family medicine physician of today.

Increasingly, these health care professionals are caring for rural populations that the U.S. Agency for Healthcare Research and Quality describes as “poorer, sicker, older, uninsured, and medically underserved” compared with their urban counterparts.

The Patient Protection and Affordable Care Act has tried to level the field by extending health care coverage, particularly to vulnerable children. Although disparities in care and access have dwindled, they do remain. In mountainous areas, near pristine lakes, and throughout the vast plains of our country, people settle, build homes, and raise families—and hope they do not need to visit a faraway hospital or receive care they cannot afford.

The Association of American Medical Colleges predicts our nation will need nearly 36,000 more primary care doctors by the year 2025 and recommends that these doctors mirror the diversity of the people they care for. At HMS, we are determined to research and address health care disparities, and we are dedicated to ensuring that our graduates reflect the diverse populations of this country. Our students share this vision; they are as passionate about social justice and health equity as they are about clinical care and medical research.

In this issue of *Harvard Medicine*, we think outside the city by exploring rural health care in the United States.

George Q. Daley
Dean of Harvard Medical School

Harvard Medicine

Editor

Ann Marie Menting

Design Director

Paul DiMattia

Assistant Editor

Susan Karcz

Senior Graphic Designer

Jill Carrico

Contributing Writers

Eric Bender, Jessica Cerretani, Elizabeth Dougherty, Katie DuBoff, Stephanie Dutchen, Kevin Jiang, Sue McGreevey, Jake Miller, Mike Morrison, Ekaterina Pesheva, Cuthbert Simpkins

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Phone: 617-432-7878 • **Fax:** 617-432-0446

Email: harvardmedicine@hms.harvard.edu

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Letters to the Editor

CHART NOTES FROM OUR READERS



In Tune

I was delighted to see the Winter 2017 issue of *Harvard Medicine* and your interest in connections. It is my belief that this is the key to successful medical and psychological research and treatment because a human being is not a solo artist—he or she is an orchestra.

VIRGINIA ANN VAN SETERS
COLUMBIA, SOUTH CAROLINA
MEMBER, HMS EZEKIEL HERSEY COUNCIL

Hugs for Hire

In the article “Soft Touch,” which appeared in the Winter 2017 issue of *Harvard Medicine*, I was pleased to see that kangaroo care is finally getting some “best practices” support. We need to extend kangaroo care beyond infancy.

I worked as a NICU nurse in the 1980s but now work as a school nurse. I see problems that result from allowing our children to be raised by strangers so that we can manage dual-career households. We are sending children to day care at the tender age of three to six months, and they are being raised by nonfamily members who are paid to tend to their needs.

This disturbs me.

I believe that a mother or a father needs to be the primary caretaker of young children in order to ensure their proper growth and development—just as kangaroo care does for infants.

DEBBIE GREIFF
NEEDHAM, MASSACHUSETTS

I believe that a mother or a father needs to be the primary caretaker of young children in order to ensure their proper growth and development—just as kangaroo care does for infants. Children can go to preschool at two and a half or three years of age, but it is essential that an adult, one with a vested interest in nurturing the child, remains an integral part of the raising and caring of that child during those very formative years.

DEBBIE GREIFF
NEEDHAM, MASSACHUSETTS

Giving Due

Harvard Medicine's article about the founding of the HMS Department of Neurobiology fifty years ago (Autumn 2016) specified that GABA was identified as an inhibitory neurotransmitter in lobsters. Conspicuously absent was

mention that David Hubel and Torsten Wiesel's Nobel-winning experiments were done in cats and monkeys. To understand how the human brain works, experiments must be conducted in other mammalian species. Glossing over this fact only undercuts public support for animal research.

I was a graduate student of Steve Kuffler's and, like my fellow grad students, will never forget the day in 1980 when he died. We all loved him.

JONATHAN C. HORTON '80
SAN FRANCISCO, CALIFORNIA

Take a Breath

Imagine my delight in finding “Zen” mentioned twice in the Winter 2017 issue of *Harvard Medicine*!

First, Elissa Ely '87 described the mindful meditative remedy used by Ronald Epstein '84 to soothe his own haste and stress. It was an approach that encouraged “what the Zen masters call ‘beginner's mind.’”

Later, the interview with our new dean, George Q. Daley '91, brought out that the “Zen” he achieved while fishing enabled him to relax, connect with his sons, and distance himself “from the ongoing buzz of everyday life.”

A broad, mutually illuminating interface exists between Zen and the neurosciences. Curious readers may discover more about Zen and other topics of practical biomedical interest in the series of six books I've written and had published by MIT Press between 1998 and 2016.

JAMES H. AUSTIN '48
COLUMBIA, MISSOURI

Harvard Medicine welcomes letters to the editor. Please send letters by mail (Harvard Medicine, 107 Avenue Louis Pasteur, Suite 111, Boston, MA 02115) or email (harvardmedicine@hms.harvard.edu). Letters may be edited for length and clarity.



MATCH LIST 2017

Students receive residency assignments

Justin Stevens with HMS student Erica Kiemele (left to right)

ANESTHESIOLOGY

Nicholas Alvey

University of Colorado School of Medicine*

Anna Frackman

Stanford University Programs

Elliott Hoel

University of Washington
Affiliated Hospitals*

Alisha Ling

Massachusetts General Hospital

Mckenna Longacre

Brigham and Women's Hospital*

Kai Qiu

Massachusetts General Hospital

Matthew Tung

Massachusetts General Hospital*

Elisa Walsh

Massachusetts General Hospital*

Rachel Wood

Vanderbilt University Medical
Center

DERMATOLOGY

Allison Dobry

University of California Irvine
Medical Center*

Anna Garza-Mayers

Massachusetts General Hospital*

Nicole Gunasekera

Massachusetts General Hospital*

Karyn Haitz

Jackson Memorial Hospital Miami*

Hasan Khosravi

University of Pittsburgh Medical
Center*

Jasmine Rana

Stanford University Programs*

Michael Waul

University of California San
Francisco*

Jennifer Yeh

Massachusetts General Hospital*

EMERGENCY MEDICINE

William Brown

Massachusetts General Hospital
(Brigham and Women's-Harvard)

Mia Geurts

Madigan Army Medical Center

Kelsy Greenwald

Massachusetts General Hospital
(Brigham and Women's-Harvard)

Edward Grom

University of California San
Francisco

Matthew Heuton

University of Chicago Medical Center

Nicholas Jensen

University of Cincinnati Medical
Center

Hazar Khidir

Massachusetts General Hospital
(Brigham and Women's-Harvard)

Erica Kiemele

University of Southern California

Lucinda Lai

Massachusetts General Hospital
(Brigham and Women's-Harvard)

Bennett Lane

University of Cincinnati Medical
Center

Melanie Molina

Massachusetts General Hospital
(Brigham and Women's-Harvard)

Grace Taylor

University of California San
Francisco

Jessica Tsao

New York University School of
Medicine

FAMILY MEDICINE

Daniela Delgado

Harbor-UCLA Medical Center

Alexandra Gast

Boston University Medical Center

Sara Martin

Sutter Medical Center Santa Rosa

Viet Nguyen

University of Washington
Affiliated Hospitals

Anne Marie Williams

Swedish Medical Center

GENERAL SURGERY

Grace Chao

Yale-New Haven Hospital

Sam Dubal

Harbor-UCLA Medical Center

Ryan Eton

University of Michigan Hospitals

Morgan Hennessy

Massachusetts General Hospital

Lenka Ilcinis

Brigham and Women's Hospital

Ariana Metchik

Georgetown University Hospital

Cynthia Miller

Massachusetts General Hospital

Samia Osman

Beth Israel Deaconess Medical
Center

Irene Zhang

University of Washington
Affiliated Hospitals

INTERNAL MEDICINE

Omar Bayomy

Brigham and Women's Hospital

Kirsti Campbell

Brigham and Women's Hospital

Aaron Cohen

Brigham and Women's Hospital

Helen D'Couto

Massachusetts General Hospital

Aaron Deutsch

Brigham and Women's Hospital

Ashley Dickens

Massachusetts General Hospital

Darja Djordjevic

Mount Auburn Hospital

Sarah Englehart

University of Toronto

Ofer Fass

New York University School of
Medicine

Joshua Foromera

University of Colorado School of
Medicine

Tiara Forsyth

Massachusetts General Hospital

William Gibson

Brigham and Women's Hospital

George Huang

Brigham and Women's Hospital

Nina Jain

Brigham and Women's Hospital

Christopher Kearney

Massachusetts General Hospital

Komal Kothari

New York-Presbyterian Hospital /
Columbia University Medical Center

Wilson Kuswanto

Stanford University Programs

Daniel Lage

Massachusetts General Hospital

William Lewis

University of California Los Angeles
Medical Center

Stephanie Lin

Brigham and Women's Hospital

Justin Lo

Vanderbilt University Medical Center

Wilfredo Matias

Brigham and Women's Hospital

Jared Mayers

Brigham and Women's Hospital

Megan McLaughlin

University of California San Francisco

Chijioke Nze

Brigham and Women's Hospital

Krishna Prabhu

University of Washington
Affiliated Hospitals

Avanthi Raghavan

Massachusetts General Hospital

Lisa Rotenstein

Brigham and Women's Hospital

Emily Simons

University of Colorado School of
Medicine

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Massachusetts General Hospital

Anjali Thakkar

University of California San Francisco

Ramkumar Venkateswaran

Brigham and Women's Hospital

Susan Wang

Dartmouth-Hitchcock Medical Center

Joshua Wong

Stanford University Programs

Luyi Xu

Massachusetts General Hospital

Aaron Yeoh

Stanford University Programs

MEDICINE-PRIMARY

Danielle Bäck

Massachusetts General Hospital

Colleen Farrell

New York University School of
Medicine

Carly Hudelson

University of Washington
Affiliated Hospitals

Brian Powers

Brigham and Women's Hospital
(Harvard Vanguard Medical
Associates)

Aaron Schwartz

Brigham and Women's Hospital
(Harvard Vanguard Medical
Associates)

Shanna Tucker

New York Presbyterian Hospital /
Weill Cornell Medical Center

Ana Sofia Warner

Massachusetts General Hospital

NEUROLOGICAL SURGERY

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University of California Los
Angeles Medical Center

Michelle Chua

Saint Joseph's Hospital Phoenix

NEUROLOGY

Christine Eckhardt

Brigham and Women's Hospital*
(Massachusetts General Hospital)

Tova Gardin

Yale-New Haven Hospital*

Jill Goslinga

University of California San Francisco

Alexis Roy

Brigham and Women's Hospital*
(Massachusetts General Hospital)

Priya Srikanth

Brigham and Women's Hospital*
(Massachusetts General Hospital)

OB/GYN

Ida Bernstein

Brown University / Women and
Infants Hospital

Sarah-Bianca Dolisca

Brigham and Women's Hospital
(Massachusetts General Hospital)

Bridget Donovan

Brigham and Women's Hospital
(Massachusetts General Hospital)

Taylor Freret

Brigham and Women's Hospital
(Massachusetts General Hospital)

Leigh Humphries

Hospital of the University of
Pennsylvania



Jill Goslinga

Amy Le
Kaiser-Permanente San Francisco

Benjamin Matthews
Boston University Medical Center

Nina Woolley
University of Pittsburgh Medical Center

OPHTHALMOLOGY

Joseph Anaya
Wills Eye Residency*

Emily Gross
University of Michigan Ann Arbor*

Clifford Kim
Massachusetts Eye and Ear*

Yingna Liu
University of California San Francisco*

ORAL AND MAXILLOFACIAL SURGERY

Ami Amini
Massachusetts General Hospital

Jeffrey Hajibandeh
Massachusetts General Hospital

Mark Rowan
Massachusetts General Hospital

ORTHOPAEDIC SURGERY

Lauren Barber
Hospital for Special Surgery

Arthur Bartolozzi IV
Stanford University Programs

Daniel Driscoll
Hospital for Special Surgery

Mark McElroy

University of Pittsburgh Medical Center

Matthew Tarabochia

Massachusetts General Hospital

John Zhao

Massachusetts General Hospital

PATHOLOGY

Melis Anahtar

Massachusetts General Hospital

Mitra Dowlatshahi

New York-Presbyterian Hospital /
Columbia University Medical Center

Cindy Schmelkin

Brigham and Women's Hospital

Michael Susman

Vanderbilt University Medical Center

PEDIATRICS

Alona Birjiniuk

Baylor College of Medicine

Zoe Bouchelle

Children's Hospital of Philadelphia

Kathryn Brubaker

Massachusetts General Hospital

Robert Crutcher

Walter Reed National Military
Medical Center

Margaret Fallon

Massachusetts General Hospital

Laurel Gabler

Children's Hospital of Philadelphia

Nathan Georgette

University of Chicago Medical
Center

Vera Goldberg

University of California San
Francisco*

Divya Jayaraman

Boston Children's Hospital
(neurology)

Brandon Kappy

Cincinnati Children's Hospital

Carl Malm

Yale-New Haven Hospital

Amanda Marinoff
Boston Children's Hospital

Alexandra Power-Hays
Boston Children's Hospital*
(Boston Medical Center)

Anna Ruman
Massachusetts General Hospital

Ann Symonds
Icahn School of Medicine at
Mount Sinai

Marguerite Thorp
University of California Los Angeles
Medical Center

Leah Wibecan
Massachusetts General Hospital
(neurology)

PHYSICAL MEDICINE AND REHABILITATION

Cameron Olezene
Spaulding Rehabilitation Hospital*

PLASTIC SURGERY

Luccie Wo
Jackson Memorial Hospital Miami

PRELIMINARY SURGERY

Rahul Sastry
Brigham and Women's Hospital

PSYCHIATRY

Olusola Ayankola
Yale-New Haven Hospital

Noor Beckwith
Massachusetts General Hospital

Devin Cromartie
Boston University Medical Center

Carolyn Gaebler
Cambridge Health Alliance

James Luccarelli
Massachusetts General Hospital

Sara Powers
Maine Medical Center



Dean for Students Fidencio Saldaña (center, rear) with Paris Tucker and HMS students Shanna Tucker and Victor Babatunde (front, left to right).

Rachael Rosales
Brigham and Women's Hospital

RADIATION ONCOLOGY

Idalid Franco
Massachusetts General Hospital*
(Brigham and Women's-Harvard)

Katie Hwang
Massachusetts General Hospital*
(Brigham and Women's-Harvard)

Sumi Sinha
University of California San
Francisco*

Shervin Tabrizi
Massachusetts General Hospital*
(Brigham and Women's-Harvard)

RADIOLOGY

Victor Babatunde
Hospital of the University of
Pennsylvania*

Daniel Chonde
Massachusetts General Hospital*

Jeffrey Cooper
Duke University Medical Center*

Julia Mario
Brigham and Women's Hospital*

Colette Martin
Brigham and Women's Hospital*

Gregory Parker
Hospital of the University of
Pennsylvania*

Andrew Taliaferro
University of California San
Francisco*

UROLOGY

Gricelda Gomez
Brigham and Women's Hospital*

Albert Ha
Columbia College of Physicians and
Surgeons*

OTHER

Christiana White Beveridge
Associate Consultant
McKinsey & Company

Luciano Custo Greig
Beth Israel Deaconess Medical
Center*

Andrew Le
CEO Buoy Health Austin

Gaurie Tilak
Consultant
McKinsey & Company

INSTITUTIONS listed represent categorical residency matches and their locations. Listings marked with an asterisk (*) indicate preliminary or transitional programs that may or may not take place at the locations of the categorical residencies. Jointly administered programs are noted in parentheses.



Model of human insulin

They Divide to Conquer

Why do insulin-producing beta cells often fail to proliferate in people with diabetes?

RESEARCHERS HAVE LONG SOUGHT to understand why insulin-secreting beta cells in the pancreas often fail to proliferate in people who go on to develop type 2 diabetes. Studying both humans and mice, HMS scientists at Joslin Diabetes Center now have identified one key biological mechanism that can prevent successful cellular division. Their study was published April 4 in *Cell Metabolism*.

"Very often," says Rohit Kulkarni, an HMS professor of medicine, a Joslin senior investigator, and senior author of the study, "many of the beta cells that begin the cell cycle don't complete it because the regulatory signals aren't appropriate. The cells instead choose to die."

Kulkarni's lab had previously analyzed beta cells that were modified to lack an

insulin receptor and didn't divide as easily as normal beta cells. They found that, compared with normal beta cells, these cells generated significantly smaller amounts of two proteins that partner to help separate the cell's chromosomes before cell division.

In their latest research, the Joslin team explored the actions of the two proteins—centromere protein A (CENP-A) and polo-like kinase-1 (PLK1)—in mice and in cells from humans and mice.

They found that mice that lacked the CENP-A protein could not compensate for insulin resistance by making more insulin-secreting cells. They also found lower levels of CENP-A and PLK1 proteins in cells from human donors with diabetes compared to levels in cells from healthy donors.

To better understand how insulin signaling affects beta-cell growth, the scientists studied a pathway involving a protein that acts as a transcription factor to regulate genes by binding to their DNA regions. This protein helps drive cell proliferation and can promote the expression of CENP-A and PLK1.

"We found that insulin signaling can initiate the binding of this transcription factor with CENP-A and PLK1, in both mouse and human beta cells," Kulkarni says. "This binding is lost in beta cells lacking the insulin receptor, and the loss of binding leads to cell death."

This type of regulation, say the researchers, is specific to beta cells and not seen in other metabolic cell types such as liver and fat cells.

—Eric Bender

Small Talk

Scientists monitor crosstalk between intestinal microbes and the immune system

THE HUMAN GUT is home to some 100 trillion bacteria, comprising between 250 and 500 species. Known as the gut microbiome, this microbial collective is a powerful regulator of disease and health and has been implicated in conditions ranging from inflammatory bowel disease to multiple sclerosis.

Gut microbes engage in an intricate conversation with the immune system, stimulating it just enough to keep disease-causing invaders at bay, while at the same time checking it so it doesn't mistakenly attack the body. So far, scientists have been able to pick up only bits and pieces of that conversation.

Now, scientists from HMS have managed to "listen" to the crosstalk between individual microbes and the immune cells and genes expressed in the gut. They did this by focusing on one microbe at a time and deciphering its effects on nearly all immune cells and intestinal genes, an approach that yielded a more precise understanding of the interplay between individual gut microbes and their hosts.

The experiments, published February 23 in *Cell*, provide a blueprint for identifying microbial influencers of disease and health, one that can help scientists screen for molecules or bacterial strains that can be used therapeutically to fine-tune certain immune responses.

"We set out to map interactions between bacteria and the immune system," says senior investigator Dennis Kasper, an HMS professor of medicine and microbiology and immunobiology, "and hoped that could eventually lead to the development of an apothecary of agents tailored to modulate the immune system selectively and precisely."

For the work, Kasper's microbiology team collaborated with HMS immunologists Diane Mathis and Christophe Benoist.

"This research took place at the intersection of microbiology, immunology, and genetics," says Mathis, an HMS professor of microbiology and immunobiology. "It illustrates the complex and synergistic ways in which multiple organs and organ systems operate in the body."

Says Benoist, an HMS professor of microbiology and immunobiology, "Because we observed microbial effects mainly in the gut, we think that a microbe-based therapy would avoid the collateral damage seen with drugs that wipe out classes of the body's immune cells."

Modulating the gut immune system, Benoist adds, may also have broader beneficial effects because gut immunity has been linked to several autoimmune diseases, including rheumatoid arthritis, Crohn's disease, and diabetes.



For the experiments, the team collected fifty-three common bacterial species from human guts and seeded them in sterile mouse guts, one microbe at a time. Two weeks later, the scientists performed immune and genomic analyses, comparing the results with those from mice whose guts were completely microbe-free. Scientists assessed each microbe's effects on twenty-one types of immune cells and on the activity of all the genes that regulate intestinal immunity.

Each immune cell type was affected by bacteria in a range of ways. Some bacteria boosted the activity of certain cells, while others dampened the activity of the very same cells. These oppositional effects, the researchers say, suggest an evolutionary checks-and-balances mechanism to ensure that no single bacterium can overpower the others in its effects on the immune system.

Similarly, some bacteria upregulated certain genes, while others

downregulated them, indicating that microbes can help balance intestinal gene expression.

A quarter of the fifty-three bacteria studied boosted the census of regulatory T cells, which are responsible for taming inflammation and which help shield the body from self-inflicted immune assault.

The researchers also note that a single little-known microbe, *Fusobacterium varium*, had the most powerful effect on immune cells, including the suppression of naturally secreted antimicrobials and the ability to turn on several genes that promote inflammation.

The class of immune cells most affected was plasmacytoid dendritic cells, known to affect the function of regulatory T cells and the secretion of interferons, naturally occurring proteins that fend off viruses. Thirty-eight percent of microbes boosted the levels of these dendritic cells, while 8 percent lowered them.

—Ekaterina Pesheva



Make Way

Having a heart attack near the route of a major race decreases survival odds

PEOPLE WHO SUFFER heart attacks or cardiac arrests in the vicinity of an ongoing major marathon are more likely to die within a month as a result of delays in transport to nearby hospitals, according to HMS researchers. The delays, they say, likely stem from widespread street closures that can hamper transportation in an emergency.

In the April 13 issue of the *New England Journal of Medicine*, the authors call for citywide strategies that ensure uninterrupted access for medical crews within a certain radius of races, parades, and other large public gatherings.

"We have traditionally focused medical preparedness and emergency care availability to address the needs of race runners," says the study's senior author, Anupam Jena, the Ruth L. Newhouse Associate Professor of Health Care Policy at HMS, "but our study suggests that effects of a marathon may spread well beyond the course of the event."

The investigators examined 10 years' worth of patient

records analyzing death rates among those 65 years of age and older, within 30 days of having a heart attack or a cardiac arrest near a major marathon across eleven U.S. cities. They compared death rates among patients hospitalized on race day with those of patients hospitalized five weeks pre- and post-race. Additionally, the researchers divided patients by zip code, comparing death rates among those living near the marathon with rates of those living in zip codes well outside of the event's radius and thus unaffected by street closures.

Patients admitted to a hospital on race day were nearly 15 percent more likely to die within a month of suffering a heart attack or cardiac arrest compared with those admitted on a nonmarathon day or to a hospital outside of a marathon's zip code area.

That spike translated into a nearly 4 percent increase in deaths among cardiac patients in marathon-day hospitals within the 30-day period. Thus, for every 100

patients with heart attack or cardiac arrest, three to four more people died within a month in the group admitted to a hospital on race day if they happened to go to a hospital near a race's course.

The research also showed that ambulance transport was delayed by a little more than 4 minutes on marathon days, a 32 percent longer travel time compared with transports not delayed by marathons. Additionally, nearly a quarter of patients in the study got to the hospital without an ambulance. Although there are no records of the amount of time private transportation took, the authors suspect that many such trips would also have been delayed on marathon days.

The findings do not establish cause and effect between street closures and greater mortality, yet the researchers note that many studies have shown that even very small delays in getting care for cardiac arrest or heart attack can mean the difference between life and death.

—Jake Miller

E-Z Pass

Many physicians choose insomnia meds based on habit

CLINICAL DECISION MAKING IS A COMPLEX PROCESS driven by multiple factors, including social dynamics, peer pressure, and even exposure to drug advertising. Now, research from HMS shows that a physician's choice of insomnia medication is often based on habit.

The results suggest that many clinicians choose insomnia drugs based on routine rather than by taking into account a patient's symptoms and medical history, with a physician's past prescribing pattern, rather than patient characteristics, as the best predictor of which insomnia medication a patient might get.

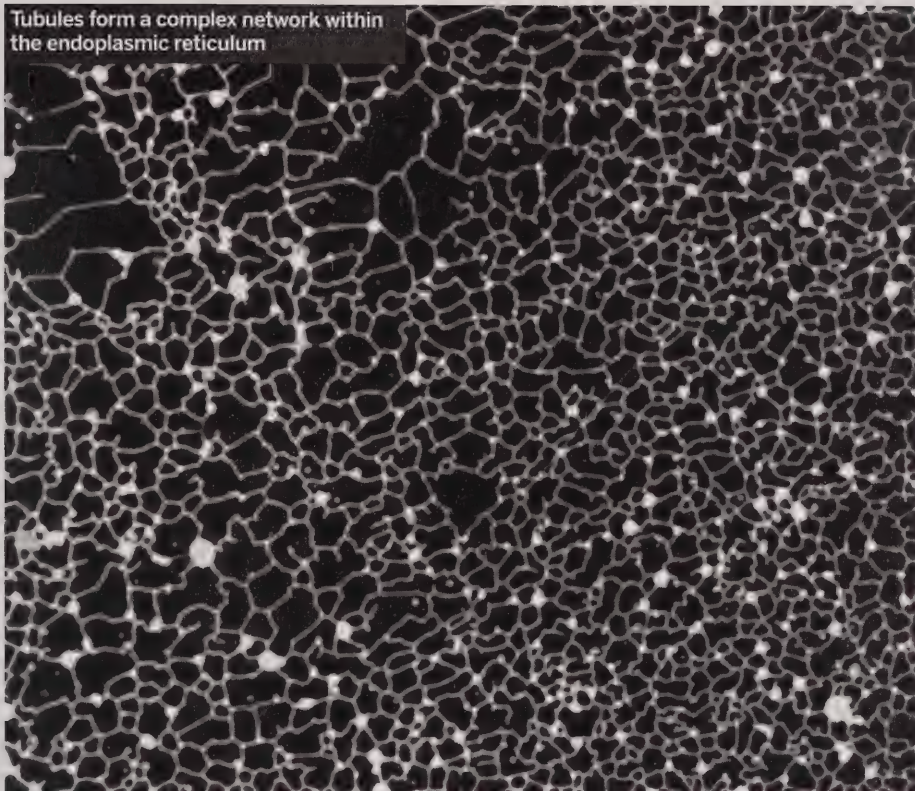
The findings appeared February 9 in *Scientific Reports*.

"Our results show that, like others, many physicians are creatures of habit who tend to rely on cognitive shortcuts in their decision making," says first author Andrew Beam, a postdoctoral research fellow in the Department of Biomedical Informatics at HMS.

Insomnia's economic burden is estimated to top \$60 billion a year in this country, a number that doesn't account for the physical toll of a condition thought to affect nearly 40 percent of the U.S. population. Yet insomnia remains underdiagnosed and poorly treated.

The researchers focused on the two most commonly prescribed drugs: zolpidem, a newer medication with a great efficacy record but associated with side effects such as next-day drowsiness and dizziness, and trazodone, an older drug typically used for depression and less effective for insomnia but with a well-established safety profile. After analyzing thousands of patient records and clinical notes and comparing them against each physician's prescribing records, the researchers found that a doctor who prescribed one medication in the past was three times more likely to continue prescribing the same drug. Patients who had symptoms of depression in addition to their insomnia, however, were somewhat more likely than those without depression to receive a prescription for trazodone. —Ekaterina Pesheva

Tubules form a complex network within the endoplasmic reticulum



It's Tubular

Researchers determine how part of the endoplasmic reticulum gets its shape

FROM THE DOUBLE MEMBRANE enclosing the cell nucleus to the deep infolds of the mitochondria, each organelle in our cells has a distinctive structure that makes it ideally suited to do its job. How these shapes arise, however, is largely a mystery.

Cell biologists at HMS have now determined that just three ingredients are needed to form the complex network of tubules which, together with structures that resemble stacked sheets, make up the internal architecture of the cellular organelle known as the endoplasmic reticulum. The ER makes fat and protein for the cell.

According to Tom Rapoport, an HMS professor of cell biology and leader of the study team, producing the ER's tubular network is "surprisingly simple," requiring just three ingredients. The team's findings were reported online February 22 in *Nature*.

In addition to answering a longstanding question about basic biology, the findings help explain how certain genetic mutations in ER proteins lead to hereditary progressive muscle disorders of the lower limbs, known collectively as spastic paraplegias.

"Explaining a disease doesn't mean we can cure it," says Rapoport, "but it's gratifying to trace back a complex group of diseases to a molecular defect of individual proteins."

Tubules are highly curved, with O-shaped cross sections. The researchers found that formation of the ER's tubular network engages two proteins in a continual tug of war to maintain the right amount of curvature.

Using a simple, yeast-based system they constructed, Rapoport team's found that either of two protein families—reticulons and REEPs (receptor expression-enhancing proteins)—can stabilize the curvature. The team then figured out that enzymes called GTPases help the tubule membranes stick together to form a network.

Rapoport's team went on to show that vertebrates may need even fewer ingredients than yeast: a fruit fly GTPase, atlastin, took care of both fusion and curvature stabilization, eliminating the need for a REEP or a reticulon.

—Stephanie Dutchen

THE KINDEST CUT

Scientists find control center for DNA breaks during cell division

BREAKS IN DNA CAN WREAK HAVOC in the body, giving rise to cancer and other health problems. Yet sometimes cells rupture their own DNA for a good reason.

During meiosis, when cells divide to become sperm and eggs, making and repairing DNA breaks help pairs of chromosomes lock together so they can exchange genetic material and continue their transformation.

Even "good" breaks, however, need to be controlled lest they get out of hand. But what exerts that control has eluded researchers—until now.

In a study of the reproductive organs of tiny worms called *Caenorhabditis elegans*, a team of HMS scientists, led by genetics professor Monica Colaiácovo, identified a trio of proteins that staff the DNA break control center. If the same proteins operate the controls in humans, the researchers say, the findings could suggest new ways to rein in runaway DNA breaks throughout the body and possibly help avert cancer, infertility, miscarriages, and birth defects. The research was reported March 27 in the journal *eLife*.

The team found that a pair of regulatory enzymes known as polo-like kinases 1 and 2 sense when two chromosomes attach at a DNA break site. The enzymes then stick a "no more breaks needed" chemical tag onto SYP-4 proteins that are part of a zipperlike structure that holds chromosome pairs together during meiosis.

The researchers watched through a microscope as a wave of this tagging, known as phosphorylation, started at the break site then spread out along the zipper until it reached the ends of the chromosomes.

"We think this makes the chromosomes less accessible to the machinery that makes the DNA breaks," says Colaiácovo.

The researchers discovered that phosphorylation not only blocks additional DNA breaks but it also helps stabilize the zipper, which may help disseminate the "stop" signal.

Further experiments showed that, according to Colaiácovo, "when you mess up the ability to modify SYP-4, the cells never stop making double-strand breaks." As a result, worms with uncontrolled DNA breaks had problems with their eggs that led to infertility or sterility.

—Stephanie Dutchen

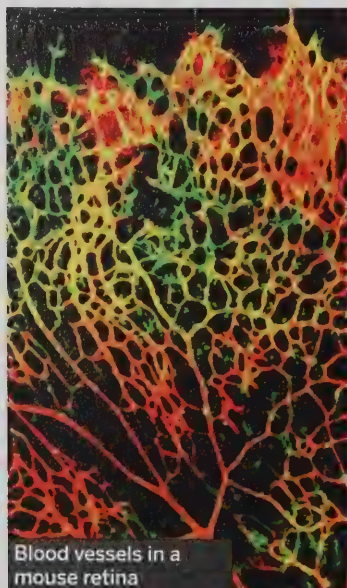
Squeeze Play

Cross-cell transport found to aid in sealing blood-retinal barrier

A CELLULAR TRAFFICKING SYSTEM called transcytosis may do most of the work in controlling the permeability of the barrier between the blood and the central nervous system, according to research conducted in mice by neurobiologists at HMS.

The findings, published March 22 in *Neuron* by a team headed by Chenghua Gu, an HMS associate professor of neurobiology and senior author of the study, defy conventional scientific wisdom, which had held that zipperlike junctions between cells were responsible for closing off the barrier.

Barriers that keep our blood from diffusing into our brain, spinal cord, and retina evolved to prevent harmful substances from passing into the central nervous system from the bloodstream, yet this selectivity also blocks the passage of most medicines.



Blood vessels in a mouse retina

Most barrier investigations have focused on tight junctions. In recent years, however, Gu has called attention to the contributions of transcytosis, in which select molecules are transported across barrier cells in bubbles called vesicles.

Gu's study revealed that, in mice, tight junctions in the retina are already in place at birth, when the blood-retinal barrier is still permeable, but that within about 10 days, the barrier gradually seals off completely, beginning in the center of the retina and moving outward.

"When we saw that the barrier was so leaky, we figured both tight junctions and transcytosis wouldn't be formed yet," Gu says.

The researchers found, however, that in the first days after birth, barrier cells hummed with vesicles ferrying molecules from the bloodstream to the retina. Yet by day 8, traffic had significantly slowed, and by day 10, it had crawled nearly to a halt. This plunge in transcytosis mirrored the pattern of barrier closure, spreading outward from the center of the retina.

If the findings are ultimately replicated in humans, whose blood-brain barrier forms before birth, they could lead to new avenues for opening the barrier to deliver drugs or tightening the barrier to treat retinal diseases and certain neurodegenerative diseases where barrier defects precede neuron death, including Alzheimer's disease, ALS, and multiple sclerosis.

—Stephanie Dutchen



SNEEZE SHIELD

Daily or weekly dose of vitamin D helped those with significant deficiency

A NEW GLOBAL COLLABORATIVE STUDY HAS CONFIRMED that vitamin D supplementation can help protect against acute respiratory infections. The study, a meta-analysis of twenty-five randomized controlled trials that included a total of more than 11,000 participants, was published online in February in *The BMJ*.

"Most people understand that vitamin D is critical for bone and muscle health," says Carlos Camargo, an HMS professor of emergency medicine, a member of the Department of Emergency Medicine at Massachusetts General Hospital, and the study's senior author. "Our analysis has also found that it helps the body fight acute respiratory infection, which is responsible for millions of deaths globally each year."

Several observational studies, which track participants over time without assigning a specific treatment, have associated low vitamin D levels with greater susceptibility to acute respiratory infections. A number of clinical trials have been conducted to investigate the protective ability of vitamin D supplementation; some found a protective effect, others did not. Meta-analyses of these trials, which aggregate data from several studies that may have different designs or participant qualifications, also had conflicting results.

To resolve these discrepancies, the research team, led by Adrian Martineau at Queen Mary University of London, conducted an individual-participant data meta-analysis of trials in more than a dozen countries, including Canada, the United Kingdom, and the United States. While traditional meta-analyses compare average data from all participants in each study, individual-participant data meta-analysis separates data from each participant, producing what could be considered a higher-resolution analysis of the data from all studies.

The investigators found that daily or weekly supplementation halves the risk of respiratory infection for individuals with the most severe vitamin D deficiencies. They also found that all participants experienced some beneficial effects from regular vitamin D supplementation. Administering occasional high doses of vitamin D did not produce significant benefits.

—Sue McGreevey and Mike Morrison



Rural Health Care

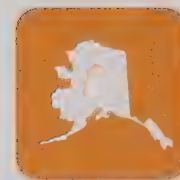
SUPPLY DROP: Making health care more accessible to rural residents sometimes requires ingenuity. One example of novel thinking is using drones to deliver medical supplies to physicians working in remote locations.

From hospitals to elder care to clinical trials, physicians and researchers are thinking outside the city

pages 14–40



LAST FRONTIER: Marna Schwartz is a pediatrician in southeastern Alaska.



In a Big Country

How doctors are tackling the health care disparities that challenge our nation's rural residents by Kevin Jiang

Almost every week, weather permitting, Marna Schwartz '00 hops into a small plane and travels from her home in Juneau, Alaska, to spend a few days seeing patients in Alaska Native and non-native communities. Life in these villages is a stark contrast to the comparatively metropolitan Juneau. Populations range from 400 to 2,500; most are accessible only by boat or plane. One of the villages that Schwartz serves has a single store and no restaurants. But it does have a community health center.

PHOTO: MICHAEL WOOD

In

this community, one of the nicest buildings is probably the clinic," says Schwartz, a pediatrician with the Southeast Alaska Regional Health Consortium, "There's going to be an x-ray machine and a little lab. It will have someone on call 24/7. The residents actually have pretty incredible access to care given the size of the community."

As in most rural areas, there is a shortage of health care workers—only two of the seven communities Schwartz regularly visits have family practice doctors. Many clinics are instead staffed by nurse practitioners and physician assistants who can diagnose, treat, and prescribe on their own or by telephone or text-based consultations with physicians in larger communities. As in most rural areas, facilities like these are crucial.

Seventeen hundred miles away as the crow flies, Matthew Tobey spends a quarter of each year seeing patients on the Rosebud Indian Reservation in southern South Dakota, an ocean of hills and grasslands that is around one-and-a-half times the size of Rhode Island and home to roughly 10,000 people. Tobey, an HMS instructor in medicine at Massachusetts General Hospital, is also associate program director of the hospital's Rural Health Leadership Fellowship program.

Last summer, the thirty-five-bed Indian Health Service hospital in Rosebud reopened its emergency room, which had been shuttered by the federal government owing to safety and staffing issues. The restoral brought much-needed relief for residents, who for months had traveled around 50 miles to get to one of two hospitals with emergency services. Hard on the heels of that relief, however, came new losses. A key clinician died, and maintenance problems and a nursing shortage forced the Rosebud hospital to close its surgery and obstetrics departments. The clinician position has yet to be filled, and the operating rooms remain closed.

Communities like those that Schwartz and Tobey serve are not simply isolated—they are underresourced.

"As soon as you fix one problem, two or three more crop up," Tobey says. "There just aren't enough human or financial resources to keep everything under control."

The Rosebud reservation spans some of the poorest counties in the nation. Eighty-three percent of tribal members are unemployed, while in the counties the reservation covers almost half of all residents live below the federal poverty level and one in six people are uninsured. Mortality rates for cardiovascular diseases, cancer, injury, suicide, and substance abuse are all significantly higher than U.S. averages. All told, life expectancy is nearly equivalent to that found in North Korea.

Permutations of this story of health disparities can be found throughout the land. Residents of remote or sparsely populated rural communities appear to be worse off than those in urban areas in almost every major statistical measure of health. People who live in rural areas have higher mortality rates in each of the leading causes of death in the United States: cancer, heart disease, unintentional injury, stroke, and chronic respiratory disease. They are more likely to abuse alcohol and other substances, use tobacco, be obese, be uninsured, and commit suicide.

There is no single explanation for this chasm. Wealth is the strongest predictor of life expectancy and is tethered to access to health care and education and to behaviors and other social factors, each of which is also independently associated with health outcomes. These social factors reflect universal challenges—the struggle for economic opportunity, for fair treatment, for hope for the future. But people living in rural regions of the United States, despite their vastly different histories and cultures, economies and geographies, share the common burden of isolation. Geographically, economically, and socially removed from urban centers that produce and consume the vast majority of the nation's resources, those who live in rural areas face additional barriers that make these challenges even more burdensome.

Going It Alone

Under the broadest definition, only 3 percent of the nation's total land area is inhabited by enough residents—at least 2,500 on a given tract of land—to be desig-



nated as an urban area or cluster by the U.S. Census Bureau. What falls outside this official definition—a mosaic of plains and mountains, coastline and desert, forests and swamps that together span an area almost the size of China—is homogeneously dubbed rural.

About one in every five people who live in the United States reside in rural parts of the country. Yet, a little more than a century ago, more than half of the U.S. population lived in rural areas. This population shift has coin-



Shelly Greenfield

Residents of remote or sparsely populated rural communities appear to be worse off than those in urban areas in almost every major statistical measure of health.

cided with, and been driven by, decades of sweeping social, economic, and technological upheavals that have increasingly concentrated financial and human capital in urban centers and amplified the isolation of rural communities.

The effects of this isolation on health care extend beyond proximity to facilities; they also affect access to specialty services.

There are almost nine times as many specialists per capita in urban areas as

there are in rural areas. As a pediatrician, Schwartz primarily serves as a consultant, offering much-needed advice and support to local providers. But complex cases must be referred to better-resourced hospitals, often in Anchorage or Juneau. For patients and their families, the time and resources needed for travel can influence their decisions on whether to pursue medical care.

“If your child has a complex behavioral, neurodevelopmental, or motor, speech, or social delay, but you don’t have local access to services for such conditions,” says Schwartz, “you may wonder why you should put a lot of effort into getting a diagnosis. If accessing a specialist means a small plane ride, a jet trip, two overnight stays, patients may choose to rely on nonspecialists who provide care in their community.”

A World of Pain

Distance to specialty care services can have wide-reaching consequences, particularly for chronic conditions such as depression or bipolar disorder. Regardless of location, the prevalence of mental health disorders is similar across the United States. Yet, around 90 percent of psychologists and psychiatrists and 80 percent of clinical social workers are based in urban areas. More than half of rural counties have no practicing mental health professionals.

“Mental health conditions require consistent follow-up,” says Shelly Greenfield ’86, an HMS professor of psychiatry and chief academic officer at McLean Hospital. “Patients may need to see somebody weekly for some forms of treatment, and if in the acute phase, almost daily in some instances. You can see immediately the problem for rural residents. It’s not a new phenomenon. I think, however, that the escalated prevalence of opioid use disorders has shined a light on this disparity.”

An estimated 2.5 million adults in the United States struggle with addiction to opioid drugs, including prescription painkillers and heroin. Opioid-related overdoses caused more than 33,000 deaths in 2015—nearly equal to fatalities from traffic accidents—and rural areas have been hit especially hard. In West Virginia, home to the highest opioid overdose rate in the country, drug companies shipped some 780 million doses of opioids to the state between 2007 and 2012. A single pharmacy in the town of Kermit, with a population under 400, received nearly 9 million doses of hydrocodone over a two-year period.

BIG SKY: Ear, nose, and throat specialist Phillip Key is based in Billings, Montana.



Around half of those who abuse drugs also meet the criteria for a mental health illness. Although numerous factors, including genetics, environment, and personal trauma are also involved, people with disorders such as depression or anxiety are at greater risk for substance use, which can escalate if left untreated, says Greenfield. In rural communities that struggle with poverty, that have a labor force engaged in work that carries the risk of physical injury, and that harbor social and cultural circumstances that can foster substance abuse disorders, the overabundance of opioids and lack of access to care have been devastating.

“Effective treatments, including medications and behavioral treatments, for all of these disorders exist,” says Greenfield. “There’s nothing magical about it. When there’s an effective treatment available for an illness, but whole populations can’t receive it because we can’t bring that treatment closer to them, then there’s something wrong with the system of care.”

There are promising efforts to bridge this gap, including free transport programs, better and more culturally appropriate training for mental health workers, and telemedicine—both physician-to-patient and physician-to-physician—to give rural providers immediate access to specialists. Addressing distance barriers then leaves economic ones: the ability to pay or to be reimbursed for treatments.

In 2010, the passage of the Patient Protection and Affordable Care Act launched various federal initiatives aimed at improving health care nationwide, including expanding mental health and substance abuse coverage. One of the more significant provisions for rural communities has been the expansion of Medicaid, which extended health care coverage to millions of previously ineligible low-income people. Although the overall outcomes are yet to be determined, some studies show that in states that accepted Medicaid expansion, rural hospitals and clinics saw an increase in revenue and improved chances of being profitable, both key to staying open.

The Feathers of Hope

Insurance coverage may also provide low-income communities with more than just access to treatment. Work from the National Bureau of Economic Research, which is tracking the outcomes of individuals since the inception of Medicaid more than 50 years ago, suggests that young children from low-income backgrounds who were covered

“Early childhood access to health insurance is potentially a social factor that can change the life trajectory of an individual.”

by the program had healthier and longer lives than peers without coverage. As adults, they had lower rates of mortality, including deaths related to cardiovascular disease, cancer, and suicide; were less likely to be disabled or on public assistance; and were more likely to be better educated and have higher-paying jobs.

“Early childhood access to health insurance is potentially a social factor that can change the life trajectory of an individual,” says Atheendar Venkataramani, a health economist and an HMS assistant professor of medicine at Mass General, who studies the health consequences of economic opportunity—the prospect for future social mobility.

The mechanisms linking health insurance access to long-term well-being are not well understood. It’s possible that financial support from programs such as Medicaid allows families to spend more on nutrition, education, and in other developmentally beneficial ways. After all, wealth leads to health—life expectancy can vary by more than 20 years between the richest and poorest counties in the United States. But Venkataramani has found that economic opportunity—optimism for higher-paying jobs or lower stress as a result of not needing to worry about access to health care, for example—may play a similarly important role. His recent research found that U.S. counties with higher economic opportunity levels have significantly lower mortality rates.

“My personal belief is that hope, motivation, and aspirations count for a lot in health,” says Venkataramani. “If you think there’s a strong economic future for you, the returns on investing in your health rise. You need to be healthy to take advantage of those opportunities. What I see in the clinic is that people who are hopeful about their future tend to

take positive steps for their health, and the people who aren’t are less motivated to do so.”

The Human Community

In a recent set of much-debated papers, Nobel Laureate Angus Deaton and Anne Case, both economists at Princeton University, found midlife mortality rates in this country were rising dramatically for non-college educated whites even as mortality fell among other groups. Their findings, they speculate, reflect “deaths of despair,” those from drug and alcohol abuse and suicide which smolder then ignite as job prospects and a cherished way of life dry up.

“The types of communities that people come from have a much more profound effect on their health, on their thinking, than anything a clinician does in a given visit,” Venkataramani says.

The hope and despair that attend the problems of rural health and care stem from the deeply interconnected concerns that touch every facet of life—social, economic, cultural, political, medical, historical. There is no single solution to the disparities between rural and urban health in this country, for there is no single cause. Yet those who deliver care to rural populations and those who conceive of, implement, and assess programs designed to chip away at the disparities so often fueled by isolation show no signs of giving up.

Just ask Phillip Key ’88, an ear, nose, and throat specialist in Billings, Montana, the state’s major metropolitan hub and its only city with a population over 100,000. When Key moved from Los Angeles to Billings, he found that he had to change the way he practiced medicine: he had to better understand his patients’ lives in order to effectively treat them.

“When I drilled down,” says Key, “I would find that a significant proportion of them would have other issues going on. Developing a relationship was vital.”

“The thing I like about Billings,” he adds, “is that the people I treat are my neighbors; we have very few degrees of separation. They’re way more neighbors than they are patients.”

“It’s not that I’ve felt I wasn’t accountable elsewhere,” he says. “But it’s a different accountability when you see people you’ve operated on, whose mom you’ve operated on, whose daughter you’ve cared for. You know those patients. And they know you.” ■

Kevin Jiang is a science writer in the HMS Office of Communications and External Relations.

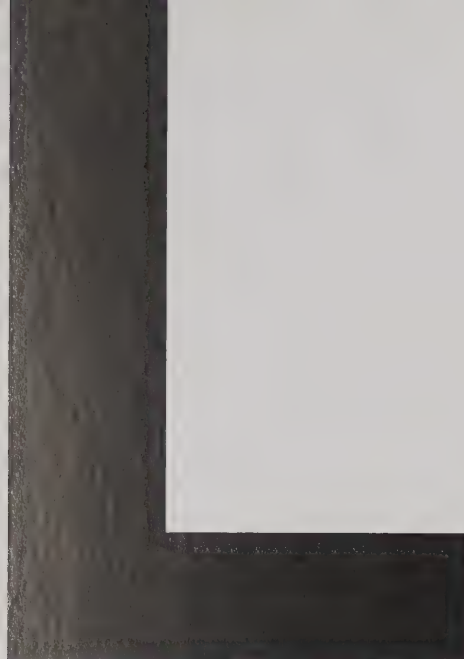


If You Build It

Rural hospitals are closing, but those that remain are reshaping and innovating by Elizabeth Dougherty

The term “rural” conjures a range of landscapes across this nation, those diamond deserts, redwood forests, golden valleys that Woody Guthrie sang belonged to all of us. ■ It is a big country, but it’s not an empty one. Twenty percent of the nation’s population lives in regions outside major metropolitan areas, according to the 2010 U.S. Census. These regions, however, are not thriving, and towns still struggle to recover from recent economic downturns. And rural residents, compared with their urban counterparts, tend to be poorer and older, to live alone, and to be without health insurance, according to the American Hospital Association.





ayered onto the challenges of living in remote locations with fragile local economies is the patchwork of health services that make up the rural health care infrastructure. This hospital system has grown organically throughout the five-decade existence of an oversight group, the Centers for Medicare and Medicaid Services (CMS). Although rural hospitals have been shaped and guided by a body of regulations, politics, and market forces, they have also been plagued by a sustainability problem, one that's familiar to any business: not enough customers.

Volume simply isn't high enough for health care economics to work.

There have been efforts to divorce hospitals from the burden of volume-based economics. In 2010, the Patient Protection and Affordable Care Act began to reward value, not volume. Many rural hospitals, however, were too small, financially tenuous, technologically bereft, or understaffed to benefit from these programs, according to a 2016 report by the U.S. Department of Health and Human Services, which focused on rural hospital participation in value-based purchasing programs. During the past few years, however, rural hospitals have begun using ACA programs and other innovations to simultaneously drive up volume and value. They've accomplished this by improving access to care, expanding capabilities, and revamping clinical decision making.

The innovations these hospitals have implemented run the gamut from value-based payment models to the use of telemedicine to provide patients with access to specialty care to new models of primary care that exist not in hospitals or doctor's offices but in retail stores. Together, these innovations have the potential to transform the current fragmented and, in some cases, crumbling, rural infrastructure into a set of flexible, capable, and interconnected systems that will best serve the medical needs of rural populations.

Fluttering Pulse

Seventy years ago, a strong economy, coupled with the practice of requiring extended bed rest during recovery from illness, injury, surgery, and childbirth, led to a hospital-building boom in this country. With medical advances, the need for extended hospitalizations—and hospital beds—has dropped, particularly in rural hospitals. So has the revenue of these hospitals.

Eighty rural U.S. hospitals have closed since 2010, a hemorrhage that began as a trickle in the 1990s. Another 673—a third of the rural hospitals in the country—are on the brink of closing, says the National Rural Health Association (NRHA). Such closures exacerbate the economic decline in rural areas: When a rural hospital closes its doors, per-capita income drops, local unemployment rises, and rural primary care doctors and nurses lose the place where they have practiced.

"If you close a hospital," says Brock Slabach, senior vice president of member services at the NRHA and a former rural hospital administrator, "you essentially terminate the employment of all the physicians and nurses in the community. Once they leave, they do not come back."

To help keep small hospitals that serve isolated rural communities afloat, a special Medicare reimbursement program, created by the 1997 Balanced Budget Act, extends additional funds to these "critical access hospitals," ensuring that emergency services remain available. Despite such support, critical access hospitals, some with just ten beds, have higher mortality rates for patients with heart attacks, heart failure, and pneumonia compared to patients in other hospitals, according to research published in the *Journal of the American Medical Association* in 2013 by cardiologist Karen Joynt, an HMS assistant professor of medicine who recently relocated to Washington University in St. Louis. In a 2011 JAMA paper, Joynt reported that these hospitals are also less likely to have intensive care units and cardiac catheterization capabilities or to have implemented electronic health records.

Joynt's research underscored the inadequacies of the rural infrastructure a fact that led many a rural doctor to contact her, voicing frustration over her findings. But Joynt says the findings also shine a light on the nearly impossible job rural hospitals are trying to do.

"Imagine being a rural emergency physician," says Joynt. "You have to know everything. On your own."

Joynt came face to face with the reality of how location can play a role in what level of care is easily available. A few years ago, her mother had a heart attack on a road trip through northwestern Nebraska. Her mother's episode happened to occur near one of the few hospitals in the region that had a cardiac catheterization lab, so she received expert care. But, Joynt adds, if that episode had occurred a few dozen miles to the south, where such facilities do not exist, her mother might not have survived.

The stakes are high for hospitals, too. For a hospital with few cases per year, a single death pushes quality statistics down. And for small rural hospitals that aren't classified as critical access, the financial risk is higher. These facilities are paid standard flat fees for episodes of care, just like their larger counterparts. Because some cases cost more while some cost less, the thinking goes that it will all balance out in the end. But for hospitals with few patients, that equilibrium doesn't exist.

"One really sick patient can close the doors," says Joynt, adding, "but we can't just give up and say rural people don't get good care. We've got to be able to think differently about this, from a systems standpoint—and from a humanistic standpoint."

Joining Forces

One promising line of systems-level thinking is the emergence of innovative ways to pay rural hospitals for the care they provide. One such is the Medicare Shared Savings Program, which encourages the formation of Accountable Care Organizations. Under this program, rural hospitals in the United States have banded together to form large, flat regional organizations.

These hospital alliances aim to save the health care system money by keeping patients in their region healthier and by preventing expensive complications. If they succeed, they collectively get a cut of the savings.

Not only do ACOs provide strength in numbers—and, in fact, an ACO must serve a base of more than 5,000 patients to qualify—they're strategic, too. The best of these rural ACOs have invested in care coordinators and population health programs designed specifically to improve care for high-cost, high-risk patients. For instance, an ACO might assign a care coordinator to focus on patients with diabetes who have a high risk for complications. The

Telemedicine use in the rural United States increased by about 28 percent annually between 2004 and 2013. One fast-growing form of telemedicine is direct-to-consumer, meaning patients dial in to doctors from home.



Ateev Mehrotra

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Lee Schwamm

prime goal is to get the disease under control and to avoid costly, and dangerous, medical episodes.

But rural hospitals need to satisfy that other goal, too: volume. When a patient visits an urban specialist and plans a series of tests, the care coordinator will direct the patient to get the tests done locally.

"Keeping care local is critically important," says Slabach. "Through care management, this system increases volumes delivered locally."

The jury is still out on ACOs, but rural ACOs seem to be doing well. The ones that formed between 2012 and 2015 cared for just 5 percent of Medicare beneficiaries, yet they accounted for more than 20 percent of the total savings in the Medicare Shared Savings Program. According to CMS, the average shared savings per ACO was more than \$4 million.

"Rural hospitals are smaller and can change quickly," says Slabach. "They can be the laboratories for this innovation."

Anytime, Anywhere

As promising as rural ACOs may be, they don't address the lack of specialists, who tend to set up shop in areas where they see a sufficient number of cases to maintain their expertise.

Telemedicine, however, brings in a specialist whenever one is needed. Telemedicine use in the rural United States increased by about 28 percent annually between 2004 and 2013, according to a 2016 JAMA paper by Ateev Mehrotra, an HMS associate professor in the Department of Health Care Policy. One fast-growing form of telemedicine is direct-to-consumer, meaning patients dial in to doctors from home.

"These services receive an estimated 1.5 million visits per year," says Mehrotra.

Yet, says Lee Schwamm '91, executive vice chairman of neurology at Massachusetts General Hospital, "with for-profit telemedicine companies, it can simply be transactional care. You get whoever's on call at the moment. If further care is required and you need to call back or transfer a patient, there's no warm handoff."

Direct-to-consumer telemedicine is a bit like calling a company's customer service line. If the problem isn't resolved by the end of that phone call, it's difficult to reconnect with the same agent. According to the Health and Medicine Division of the National Academies, some of the most egregious medical errors, and some of the poorest medical outcomes, occur when handoffs from one doctor or facility to the next are unstructured.

Some models of systematized telemedicine that are built into a system of care don't

fall into this trap. For instance, the MGH TeleStroke system, developed and directed by Schwamm, uses a hub-and-spoke network of hospitals. With Mass General at the hub, the network serves twenty-three hospitals in New England and provides rural hospitals from Maine to Martha's Vineyard with round-the-clock and near-immediate access—within 5 minutes—to expert neurologists to evaluate stroke patients.

The program has expanded the capabilities of local hospitals; they now stock brain-saving, clot-busting drugs and, guided by expert consults, staff can administer them to appropriate patients within the four-and-one-half hour window of effectiveness. The consults also help differentiate patients who can remain local for their care from those who need to be transferred to a special facility. According to 2014 metrics published by the TeleStroke group, 60 percent of patients were deemed stable enough to receive treatment close to home.

"Keeping care local is vital for small hospitals to stay in business and to lower the overall costs of health care," says Schwamm, "as long as it's care they can manage with high quality."

Similar systems have shown success for other specialties, such as mental health. "We know we can't deliver care the way we did twenty or thirty years ago," says Mehrotra. "We have to move away from the idea that health care occurs only in the doctor's office or emergency room."

Big Box Care

While these network solutions have the potential to improve care coordination and access to specialists, they don't address the dire need for primary care access in rural parts of this country. Approximately 77 percent of rural counties in the United States are so-called medical deserts, owing to a shortage of primary care professionals, according to the NRHA.

This gap is being filled, but not by traditional health care outlets. It's being filled by Walmart.

During the past decade, retail clinics have opened in drugstores and big-box stores. These clinics have a competitive edge over in-hospital clinics and doctor's offices because they offer long hours, walk-in visits, and transparent pricing and services. Mehrotra's research, in fact, suggests that the quality of care at retail clinics is at least as good as that received in doctor's offices and emergency rooms.

Most retail clinics are located in urban and suburban areas, according to a 2016 RAND report, but over the past few years, Walmart has begun opening clinics in rural areas. Today, nearly twenty Walmart Care Clinics serve predominantly rural areas in South Carolina, Georgia, and Texas.

Walmart's clinics describe themselves as primary care access points. The clinics, staffed by nurse practitioners, offer immunizations, programs to manage chronic disease, women's health screenings, and acute care.

"I think we'll see nurse practitioners become the entry point to primary care," says Sandy Ryan, a nurse practitioner and vice president of Walmart Care Clinics.

One concern is that retail clinics will provide "hit-and-run" service rather than something approximating integrated care, although Ryan says Walmart provides referrals, shares health records, and accepts a growing list of insurance plans.

What may be most compelling, however, is that Walmart appears to be reaching people who have fallen through the health care cracks. Since 2015, Walmart has sponsored free blood-pressure checks and glucose- and vision-screening events that have to date reached more than 1 million people country-wide. In January, more than 330,000 took part in the free screenings, while at a separate, one-day event, 13,000 people received immunizations. Ryan adds that the Walmart clinics' price transparency and convenience have attracted many patients who haven't been seen by a doctor in a decade or more.

Increased patient access to care could translate, through local referrals, to higher volumes for other health care outlets in a given region. Higher volumes make for a more robust business model, not to mention a healthier population.

"Any effort to bring more primary care practice outlets into rural communities is a good thing," says Slabach.

Ultimately, these innovations, if combined, could lead to the emergence of a rural health care system that is able to optimally leverage the capabilities of all of its providers and facilities.

The most important ingredient, besides continued creativity, may be patience.

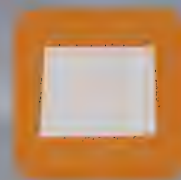
"This country is known for its incrementalism," says Slabach. "We're not going to do anything revolutionary. It's all evolutionary." ■

Elizabeth Dougherty is a Massachusetts-based science writer.



IN THE

FOREVER WEST: Natural barriers, such as the Wind River Mountains that ring ranches in western Wyoming, can complicate efforts to get to a hospital.



For three generations, Monica Bertagnolli's family has raised cattle in Wyoming. Their ranch, the White Acorn, undulates across 4,800 acres at the base of the Wind River Mountains. The family's history is twined to the land; separation is temporary, difficult, nearly inconceivable. ■ When Bertagnolli's father was diagnosed with cancer, he drove more than eight hours round trip to get care. And when her mother's abdominal aorta ruptured, she was driven over the surrounding mountains to a regional hospital. That hospital, however, didn't have any blood for transfusion, so Bertagnolli's mother was airlifted to Casper for surgery. She survived the catastrophe—the rural health care system came through for her. ■ Today, Bertagnolli, the HMS Richard E. Wilson Professor of Surgery in the Field of Surgical Oncology at Brigham and Women's Hospital, spends most of her time in the Boston area, where, among her other responsibilities, she oversees multi-institutional cancer cooperatives. Although far from Wyoming, she advocates for rural communities as she helps shape, direct, and recruit participants for clinical studies.

PICTURE

Researchers act to improve geographic diversity in clinical studies
by Stephanie Dutchen



he outreach Bertagnolli does to rural communities fills a near void. Since 1993, the National Institutes of Health has required inclusion of women and racial and ethnic minorities in clinical studies it supports. Yet even as definitions of diversity have expanded to include sexual and gender minorities, children, and the older adults, one variable still struggles for recognition: zip code.

"Nobody with cancer wants to pick up and go to a trial in Boston or Chicago if they live in a small, rural community," says Bertagnolli.

Evidence increasingly indicates that involving patients, practitioners, and investigators from rural and underresourced areas in all stages of clinical research expands access to experimental therapies, gives more people the chance to contribute to medical advancement, and uncovers differences in treatment response based on environmental and cultural factors. Encouraging diverse input also raises the likelihood that communities can implement trial protocols and the resulting standards of care.

Given Boston's chart-topping 185 trial sites per 10,000 people—nearly three times as many as the next city on the list—it would be easy for HMS to operate in an urban research bubble. Instead, the School is actively working to lower technological, cooperative, and administrative barriers to rural participation.

Trial Latitude

"We want there to be easier participation, regardless of where folks live," says Barbara Bierer '80, an HMS professor of medicine and senior vice president for research at Brigham and Women's. "I think the sweet spot lies in empowering community physicians to advance medical knowledge as far as they are able."

Studies indicate clinical trial enrollment rates among rural and underresourced communities lag behind the national average. Rural residents as a whole may be even more underrepresented in clinical research than racial and ethnic minorities. A study in Maryland flags rural residents and Blacks as the top two minority groups experiencing "serious gaps" in trial recruitment; a survey of South Carolina investigators reports that rural residents are least represented in trials and hardest to recruit, even compared to low recruitment rates in local Black communities. A 2011 analysis in the *Journal of the National Comprehensive Cancer Network* found that place of residence edges out race as a significant component in patient accrual in cancer studies, leading the authors to argue that geography should be factored into determining equitable access to clinical trials.

"Simply mapping where your patients live tells you there are big holes in some rural areas," says Isaac (Zak) Kohane, head of the HMS Department of Biomedical Informatics and principal investigator of the coordinating center for the nationwide Undiagnosed Diseases Network, which seeks diagnoses for people with unexplained conditions. "You just know there are patients who are not being helped."

Regional Flavor

In 2012, Kohane and the Harvard Catalyst | Harvard Clinical and Translational Science Center developed open-source software that could cull, anonymize, and aggregate patient data from the electronic health records (EHRs) of five participating HMS affiliate hospitals. As a check, Kohane's team used the software—called SHRINE, short for Shared Health Research Information Network—to analyze comorbidities among autism patients; the researchers confirmed previous findings.

More than 700 miles south in Winston-Salem, North Carolina, Yaorong Ge, a computer scientist who'd been following Kohane's work, wondered if SHRINE could glean useful data from the much smaller set of patient records in Wake Forest Univer-

sity's catchment area, which included rural swaths in northern North Carolina and southern Virginia. He was pleasantly surprised when the attempt worked. The results largely mirrored Kohane's, except for some reason, local patients with autism had more irritable bowel disease.

"I half-joked with Zak that maybe our Southern food was causing this spike in the data," recalls Ge, now an associate professor at the University of North Carolina at Charlotte. But the incident got him thinking.

Like Ge, researchers are starting to explore the potential ramifications that rural environments and lifestyles have on disease presentations and treatment outcomes. Studies are already searching for regional variations in treatment efficacy for bipolar disorder, schizophrenia, and cardiovascular disease.

Whether it's a condition that disproportionately affects rural residents, a national analysis of disease incidence, or a protocol involving a rare genetic mutation where the few affected patients are scattered across the countryside, doing the best science—and helping the most people—requires communication.

Fruitful Exchange

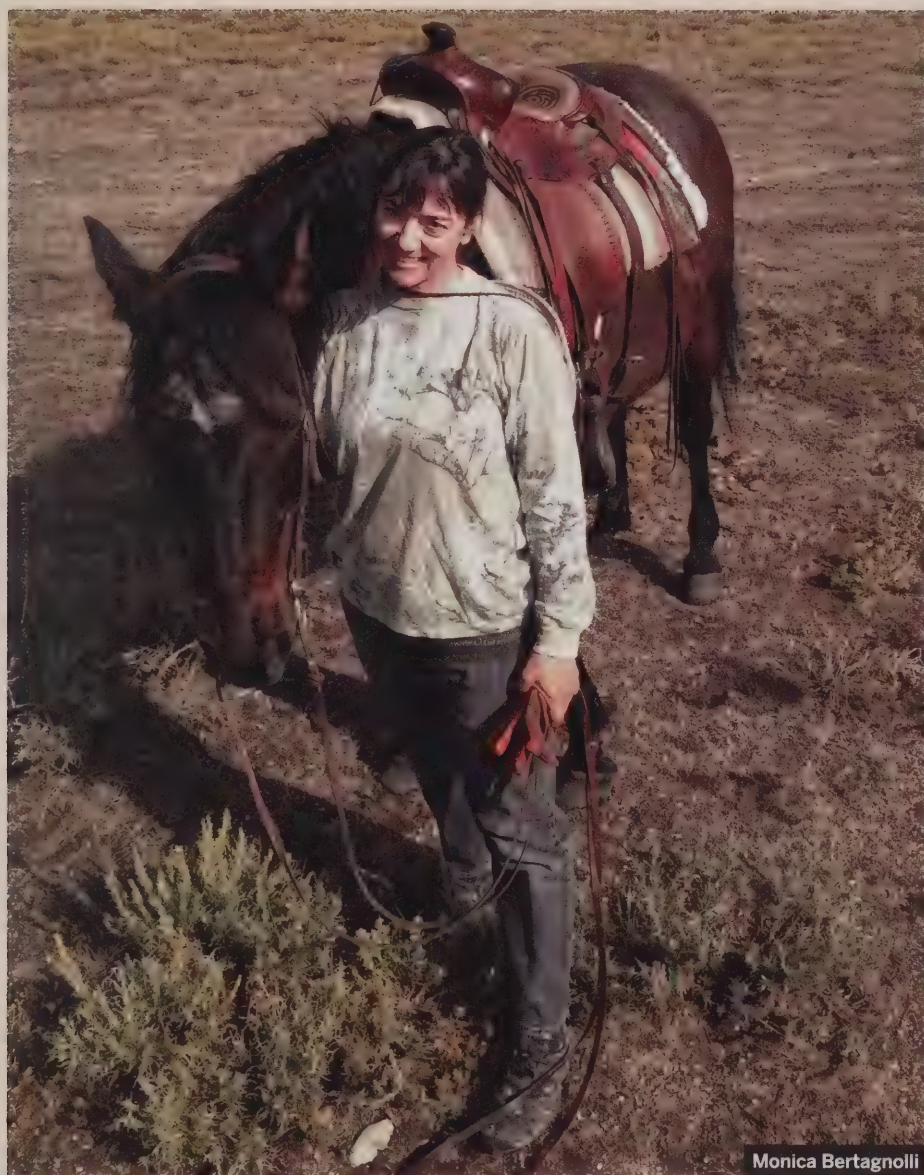
Once upon a time, academic medical centers decreed the latest trial-driven advances from their ivory towers, while community doctors adopted what they could. Now, more investigators appreciate that knowledge flows in both directions.

"Let's face it," says Bertagnolli, "if we're at an academic hospital in an urban center, our view of what it means to work with patients and put them in trials is completely different from what practitioners in Texas, for example, confront."

Bertagnolli, who will become president of the American Society for Clinical Oncology in 2018, is the group chair of the National Cancer Institute's Alliance for Clinical Trials in Oncology, a consortium that recruits half of its participants from rural sites. She makes a point of consulting community investigators about what is feasible and relevant in rural and underresourced settings.

Feedback on everything from trial design and scheduling of visits to ethics guidelines and consent paperwork helps ensure that rural sites can carry out study protocols and apply any new standards of care, that local patients are motivated to participate, and that outcome measures align with community values.

These sorts of exchanges have paid off. When Kohane proposed a study in



which patients could submit data via their smartphones, Ge worked with him to see if basic cell phones would suffice, since many patients he worked with didn't own smartphones. Similarly, when Bertagnolli oversaw a cancer genetics trial with a site in Utah that was struggling to understand why American Indian participants often missed their appointments, a local doctor mentioned that the community worked on a barter system. The trial team started giving participants specially designed paper summaries after each visit, and engagement soared.

Even as definitions of diversity have expanded to include sexual and gender minorities, children, and older adults, one variable still struggles for recognition: zip code.

The experience “taught us about making communication bridges,” says Bertagnolli. “That cohort ended up being our most adherent and enthusiastic.”

Easy as Really Difficult Pie

Listening to rural communities is a start, but communication alone won't overcome every challenge.

Compared to city dwellers, fewer rural patients and physicians are aware of available clinical trials. They may not know that tests that sound prohibitively expensive, like genome sequencing, will be covered. Communities also can have their own cultural norms for admitting to illness or permitting treatment.

Although circumstances vary, rural residents are overall more likely to be uninsured or underinsured, have lower incomes, and experience poorer health than their urban counterparts. Heap on job and family demands and it can be hard to commit to frequent appointments or travel long distances to study sites. Health issues, too, can bar rural residents from trials, a fact that has led some researchers to suggest redesigning inclusion criteria to allow more comorbidities.

The greater homogeneity of rural communities reported by the U.S. Census Bureau may even work against them when investigators seek more racial and ethnic minorities, wrote Alexandra Boer Kimball, an HMS professor of dermatology at Beth Israel Deaconess Medical Center, and colleagues in the online journal *Clinical Investigation*.

With practitioners, equipment, and facilities sparse in rural and underserved communities, limited health care infrastructure and human capital pose additional problems. Many rural clinics can't support the dedicated staff needed for patient recruitment or data and compliance monitoring. In addition, funding for NCI-sponsored studies does not reimburse sites fully for the costs of conducting the trials.

Those who still want to become investigators face intimidating application processes and accrual requirements, which can call for fifteen patients per year or more, says Gary Unzeitig, a breast surgeon and clinical researcher in Laredo, Texas, and one of Bertagnolli's go-to advisers.

“If a young partner in a small group practice is fired up about doing research,” he says, “the onus is on that individual to find a mentor or a site that will take them as an affiliate.”

Board Review

Bierer's father, a refugee who never finished high school, raised his children to value liberty, justice, and humanity. His daughter, a hematologist/oncologist, continues to pursue these ideals as an international leader in clinical research oversight, ensuring access to and the ethical conduct of clinical trials.

"I've always believed that we should engage patients and participants in a way we haven't done historically," she says. "They should be true partners in the clinical research enterprise."

Bierer recognized that one way to help more communities participate is for academic medical centers to do the heavy administrative lifting, such as centralizing IRB review.

Traditionally, institutional review boards for a proposed multisite trial would evaluate study materials against their own ethical guidelines. Trials could take years to start—or never get off the ground.

To address the problem, in 2016 Harvard Catalyst, together with Dartmouth University and the University of Wisconsin, created the Streamlined, Multisite, Accelerated Resources for Trials (SMART) IRB Reliance platform. Institutions that sign on—and more than 210 have so far—agree to use a single IRB's protocols, slashing trial launch times and throwing a lifeline to underresourced sites that don't have IRBs. Bierer, the program's director of regulatory policy, and Lee Nadler '73, dean for clinical and translational research at HMS and principal investigator of Harvard Catalyst and SMART IRB, want to expand into member sites' rural networks.

Through SMART IRB and the Multi-Regional Clinical Trials Center (MRCT) of Harvard and Brigham and Women's, Bierer and colleagues are compiling best practices for single IRB review and have developed plain-language training materials to help community partners form or join IRBs. Bierer co-founded MRCT in 2009 to improve clinical research quality worldwide.

The MRCT has also created a toolkit for communicating trial results to participants, a noticeable gap in both rural and urban research. The European Medicines Agency is adopting the kit in its forthcoming policy; Bierer hopes the United States will follow suit.

Tool Box

New technologies offer another way to bridge infrastructure gaps and collapse physical distances.



Barbara Bierer

"I've always believed that we should engage patients and participants. They should be true partners in the clinical research enterprise."

One option, telemedicine, opens doors to participation in research that involves sudden illnesses and time-sensitive treatments. Urban-based trials for acute stroke, for example, have historically struggled to enroll rural patients because the patients can't get transferred to academic medical centers quickly enough. Now, multisite trials that use telestroke networks, which allow vascular specialists to assess patients remotely, can enroll participants in community hospitals as quickly as four hours after symptom onset.

Yet while video conferencing and other high-bandwidth tools alleviate one infrastructure challenge, they bring another: According to the Federal Communications Commission, only 61 percent of rural residents have access to broadband internet, compared to 96 percent of city dwellers.

By providing additional, more accessible tools, HMS and other leaders in biomedical informatics help rural and urban investigators find patient cohorts and take advantage of the data gathered during routine care.

Like Ge in North Carolina, institutions worldwide are adapting and expanding the SHRINE tool to generate unprecedented cohort sizes and make novel discoveries in a range of diseases. They're also joining Catalyst's eagle-i, a network of academic and nonprofit institutions, to offer and request research resources.

SHRINE now powers the Scalable Collaborative Infrastructure for a Learning Health System, a \$7 million HMS project sponsored by the nonprofit Patient-Centered Outcomes

"Simply mapping where your patients live tells you there are big holes in some rural areas."



Isaac Kohane

Research Institute to assess treatment effectiveness and spur personalized medicine. The project is starting with a group of eight million U.S. patients from geographically and socioeconomically diverse areas.

Kohane and colleagues have further democratized research by convincing seven major EHR providers to be a part of Sync for Science, installing app-like software that allows patients and practitioners to sign consents and donate data in a standardized format.

"It's wonderful to think that this record system we are all linked to means we can learn from every single patient, no matter who they are or where they live," says Bertagnolli.

Sea to Sea

Progress is uneven, possibly impermanent. Shrinking federal budgets have hamstrung cooperative research groups, although public-private partnerships are starting to compensate, says Bertagnolli.

Even within his own department, Kohane says, people who think about rural patients often turn their attention to other countries. "We have, I think, blindness about the fact that there are some really underserved individuals here at home," he says.

"I'm getting older, and I'm a little worried," admits Unzeitig. He introduced clinical trials to Laredo, and he's not sure anyone in the city will take the reins when he retires. Even his daughter, heading for a breast oncology fellowship at the Mayo Clinic, seems reluctant to move back. "It happens," he says. "Sites close. One PI runs the show and when he leaves, the whole program falls apart. That's the end, and it's sad."

Bierer points out that the goal isn't necessarily for all trials to be conducted nationwide. A study attempting to shorten the length of an antibiotics course requires fewer resources than one that's evaluating a brand-new intensive cancer therapy. "We're at the threshold of developing a more refined sense of the differences among clinical trials so we can put the right support systems in the right places," she says.

But the future won't arrive until more researchers acknowledge and work to bridge the research divide between city and country, academia and communities.

"We need to recognize that this is all one big connected system," says Bertagnolli, "and both sides need each other." ■

Stephanie Dutchen is a science writer in the HMS Office of Communications and External Relations.

Rally Round

What can be done to bolster the dwindling number of rural physicians?
by Jessica Cerretani

FORWARD: In the early 1900s, building a round barn, like this one in Vernon County, Wisconsin, was considered progressive. Today, rural-based approaches to delivering quality care on a slim budget may set the stage for health care innovation throughout the nation.

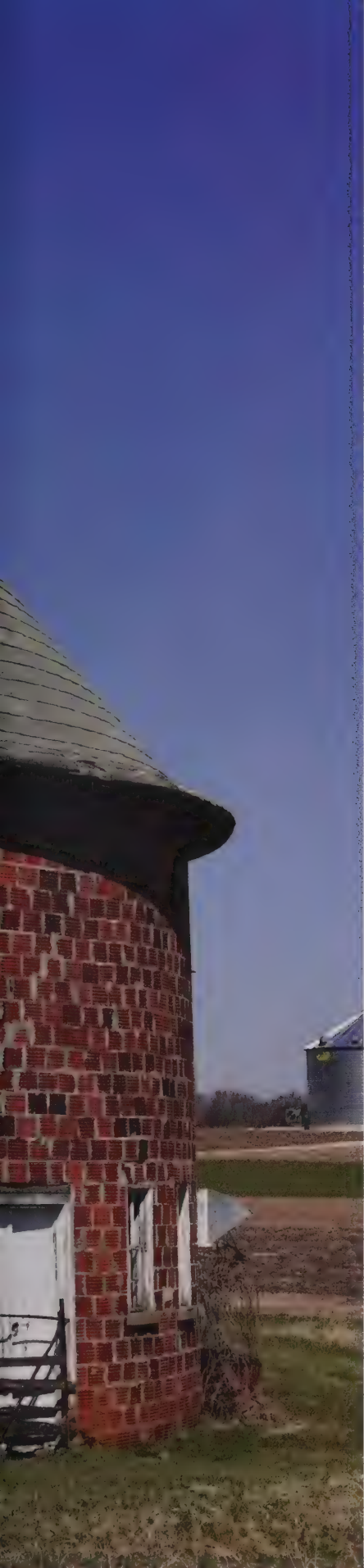


PHOTO BY WIKIPEDIA

It was the end of a long day at the clinic. As Byron Crouse latched the door behind him, he spotted a familiar face down the street. The woman waved. He shouted a friendly greeting, but didn't end it with "and how are you?" He already knew. As one of the 2,000 or so souls in Spooner, Wisconsin, Crouse wasn't just the woman's neighbor. He was also her physician.

The bond between doctor and patient is one of the perks of practicing in a rural area, says Crouse, who worked in Spooner for years before assuming his current roles as associate dean for rural and community health at the University of Wisconsin School of Medicine and Public Health and associate chair for statewide programs in that school's Department of Family Medicine and Community Health. "There's a joy and a pressure to it," he says. "It's a different kind of patient relationship because we know them as people and want to do better for them."

Yet the drive to provide optimal care for patients is increasingly challenging in rural areas all around the country. According to 2015 estimates from the U.S. Department of Agriculture's Economic Research Service, roughly 46 million people in the United States—20 percent of the population—live in rural areas. But according to the American Academy of Family Physicians (AAFP), just 11 percent of physicians choose to practice in these regions. The shortage of new primary care physicians in the nation overall is amplified in its rural areas, too. These regions average just sixty-eight primary care doctors for every 100,000 patients, compared with eighty-four per 100,000 in urban settings.

Crouse thinks the nation's rural population may be headed for what he calls a perfect storm as many of these physicians approach retirement and their patients, who are often underinsured or uninsured, age and get sicker.

The effects of this crisis are already evident: According to one estimate, there are currently more than 2,100 areas in the rural United States with shortages of health professionals, compared to 910 urban settings experiencing such shortages.

Slippery Slope

The Patient Protection and Affordable Care Act improved access to care for many living in rural areas by expanding Medicaid coverage to an estimated two million previously uninsured patients and by providing new revenue streams for rural hospitals. One analysis that looked at annual cost reports from rural and urban hospitals between 2011 and 2014 found that in states that expanded Medicaid, rural hospitals saw a greater increase in revenue from this program than urban hospitals did. These differences can likely be traced to the fact that, compared with their urban peers, a greater percentage of rural hospitals serve a greater number of low-income patients and are more likely to operate at a loss.

Now, with the fate of the ACA uncertain, rural physicians worry that their patients will suffer.

"When it comes to the way policy changes affect health care, rural patients are at the tip of the spear," says Stephen Martin '01, an associate professor of family medicine and community health at the University of Massachusetts Medical School. "When people are fearful that they can't afford to

pay, they don't seek out care—even if they can access it—for chronic conditions like heart disease, arthritis, and depression. Instead, in one of the wealthiest countries in the world, we've got millions of people living in pain, sadness, and quiet desperation.”

Because rural medicine operates on a slim margin, even small differences can have an enormous impact on physicians' ability to provide care. “I have grave concerns about proposed reforms to government-facilitated insurance coverage,” says Crouse. “I'm not confident that states will be as responsive to patients' needs. I think we're going to see a lot of uninsured rural patients, or people deciding to move out of state for cheaper care.”

Incentive Plan

On the surface, the reasons for the dearth of rural physicians seem obvious. “Most medical training takes place in cities,” says Martin, who also co-directs the Rural Health Scholars Program at UMass. “That sets doctors' expectations for care to what can be done in urban settings. It's difficult to compete with that.”

To address such issues, the U.S. government offers incentives to new physicians who choose to practice in rural areas. The National Health Service Corps (NHSC) offers scholarships that pay medical school expenses in return for a few years of service at an NHSC-approved high-need site. The group also has a loan repayment program that provides up to \$120,000 in tuition, as well as a living stipend, to medical and dental students in their final year of school who commit to providing primary care to patients in medically underserved areas, including rural communities, for at least three years. Some physician groups, such as the AAFP, worry that the NHSC may suffer if federal health care plans change.

Another government program seeks to tap more resources by looking outside the nation's borders for help. Since the mid-1990s, the Conrad State 30 Program, which is currently under Congressional review, has waived the requirement that foreign physicians return to their home countries for two years after graduating from U.S. residency programs. In exchange for this waiver—and the opportunity to receive a green card—physicians agree to practice in a medically underserved area for three years.

But incentivizing new physicians shouldn't be the only goal, says Martin. “It's not just about recruitment,” he explains. “After a few years, the question becomes, how do we get them to stay? It's not just a matter of paying them enough.”



Stephen Martin

Resource Allocation

Many of the challenges faced by rural physicians stem from a paucity of resources, both technical and professional. In large metropolitan areas such as Boston and New York and in many smaller urban and suburban areas, it's easy to take access to technological advancements for granted. In these places, if a patient needs a screening test—say, an MRI scan—her physician can refer her to a nearby medical center or to a department on another floor of the patient's home clinic. With a few keystrokes and a phone call, she has an appointment, and, in less than an hour, could be in the MRI suite.

In less-populated regions, however, a patient in need of an MRI scan may have to travel hours to the nearest hospital. That trip becomes even more difficult when you consider that patients in underserved and isolated communities can face obstacles that go beyond distance, such as a lack of public transportation or weather conditions that may make travel dangerous or roads impassable.

These challenges can have a troubling impact on the health of rural patients. One study found that for American Indian and Alaska Native people, the time between onset of heart attack symptoms and arrival at a hospital far outstrips that for any other racial or ethnic group. Research by Thomas



Thomas Sequist

Sequist '99 and his colleagues found that members of these communities are also less likely than their white peers to undergo procedures such as angioplasty or heart bypass surgery, primarily because their rural communities don't have cardiac catheterization facilities. Another study found that excessive travel time to transplant evaluation centers—often more than three hours

“Areas with substantial resource constraints have much to teach the rest of the country about how to squeeze unnecessary elements out of patient care and focus on what works.”

in each direction—does more than inconvenience American Indian and Alaska Native patients with end-stage kidney disease: It likely contributes to Sequist’s finding that American Indians are 60 percent less likely to receive a renal transplantation, compared to their white peers.

This scarcity of specialty care is one of the greatest areas of concern for rural practitioners, says Sequist, an HMS associate professor of medicine and of health care policy and the medical director of the Brigham and Women’s Hospital Physician Outreach Program with the Indian Health Service (IHS). But the scarcity may be linked to small patient populations.

“Whether in rural New Mexico or Nebraska, there just aren’t necessarily hundreds of patients with, for example, rheumatoid arthritis, in a single isolated community,” Sequist says. “Unfortunately, that means it’s hard to justify supporting and retaining a full-time rheumatologist—there just isn’t enough work.”

As a result, some of the care that would otherwise be provided by specialists can fall on the shoulders of primary care and family medicine physicians. Indeed, the same study by Sequist found that fewer than one-third of physicians in the IHS reported good access to specialty care. And that lack, in turn, produces a catch-22: more than half said that the complexity of care they were asked to manage without specialty input was greater than they thought it should be.

Often, these challenges add to an already substantial workload, setting the stage for fatigue and burnout.

“From a cost perspective, rural practices are at a disadvantage,” says Bruce Landon, an HMS professor of health care policy and a

professor of medicine at Beth Israel Deaconess Medical Center, “and they’re stretched from a human resources perspective. In many of these practices, the physician is also the IT specialist and the nurse is also the receptionist. They don’t have the economies of scale we see in urban settings.”

Worse, there’s often little backup from other physicians. “In medicine, just as in sports,” says Crouse, “you want a good bench supporting you. In rural practices, there is no bench—it’s just one physician providing care for people in multiple counties in a region.”

“What happens if that doctor moves or dies?” he adds, “When one person leaves, there’s a huge impact.”

Sequist expands on Crouse’s point. “Physicians who choose to work in rural areas are incredibly dedicated to patient care,” says Sequist, “but the community of other doctors is usually limited.”

“Rural physicians don’t just leave because they can’t afford to pay off medical school debt on a rural salary,” Sequist adds. “They leave because they want a community to turn to for professional and emotional support.”

Concerns about community extend to physicians’ families as well. Depending on their life stage, doctors and their families must determine whether a rural community is a good fit for everyone, from the quality of schools to the social and employment opportunities for other family members. If anyone in a family feels estranged from a supportive community, it’s likely the family won’t remain there long.

The Mother of Invention

Although the hardships of practicing medicine in rural areas may seem overwhelmingly complex, rural physicians often emphasize the benefits. In many ways, they say, rural regions are incubators for innovative approaches to patient care. For years, rural practitioners have been generating creative solutions to deliver quality care to patients with complex needs while operating on slim budgets and with limited staff support.

“Areas with substantial resource constraints have much to teach the rest of the country about how to squeeze unnecessary elements out of patient care and focus on what works,” says Martin. “We joke that it’s a MacGyver approach. But it can work really well. And it can give us powerful lessons for nimble and flexible care provision.”

One such approach involves hiring other health professionals to support rural physi-

cians. Community health workers can assist doctors by performing outreach within underserved areas, educating patients, and helping to ensure that residents seek out and receive care. Medical scribes can also help ease physicians’ workloads by gathering information, documenting visits, and otherwise taking on clerical tasks that can consume time needed for appointments. As a result, a physician can increase revenue by seeing more patients while also spending more time with each of them.

“Losing a doctor is a loss for everyone, so we need to keep people happy and productive,” says Crouse. “Scribes and other types of assistants can do that by improving quality of life.”

Technology can also open up new opportunities for patient care. For nearly two decades, the IHS has had a tele-ophthalmology program to screen patients for diabetic retinopathy at remote clinics without onsite vision specialists. Digital retinal images taken at the clinic are sent electronically to faraway ophthalmologists for interpretation. Feedback from specialists helps local physicians identify patients who need to travel to receive treatment or further evaluation, saving some patients unnecessary travel and controlling costs for the IHS, which pays for patients’ travel to receive outside specialty care.

Sequist and his colleagues at Brigham and Women’s are also using technology to share the expertise of HMS physicians with physicians practicing in isolated areas. As part of the hospital’s Physician Outreach Program, Sequist and others use videoconferencing to provide rural clinics in the IHS with continuing education programs, clinical consults, and case reviews. “The Indian Health Service has really innovated in the space and pushed telemedicine in ways that physicians in urban environments haven’t had to do,” says Sequist.

The Brigham and Women’s model allows for Boston physicians to volunteer their services at clinics in remote parts of New Mexico and Arizona, and for bringing rural physicians to the Boston hospital for annual training programs. Such an exchange of ideas and inspiration is one that Martin hopes to see expand throughout the country.

“We need to reach out to rural physicians, because they have a lot to teach medical students and other doctors,” he says. “They are doing remarkable work and we need to honor that experience.” ■

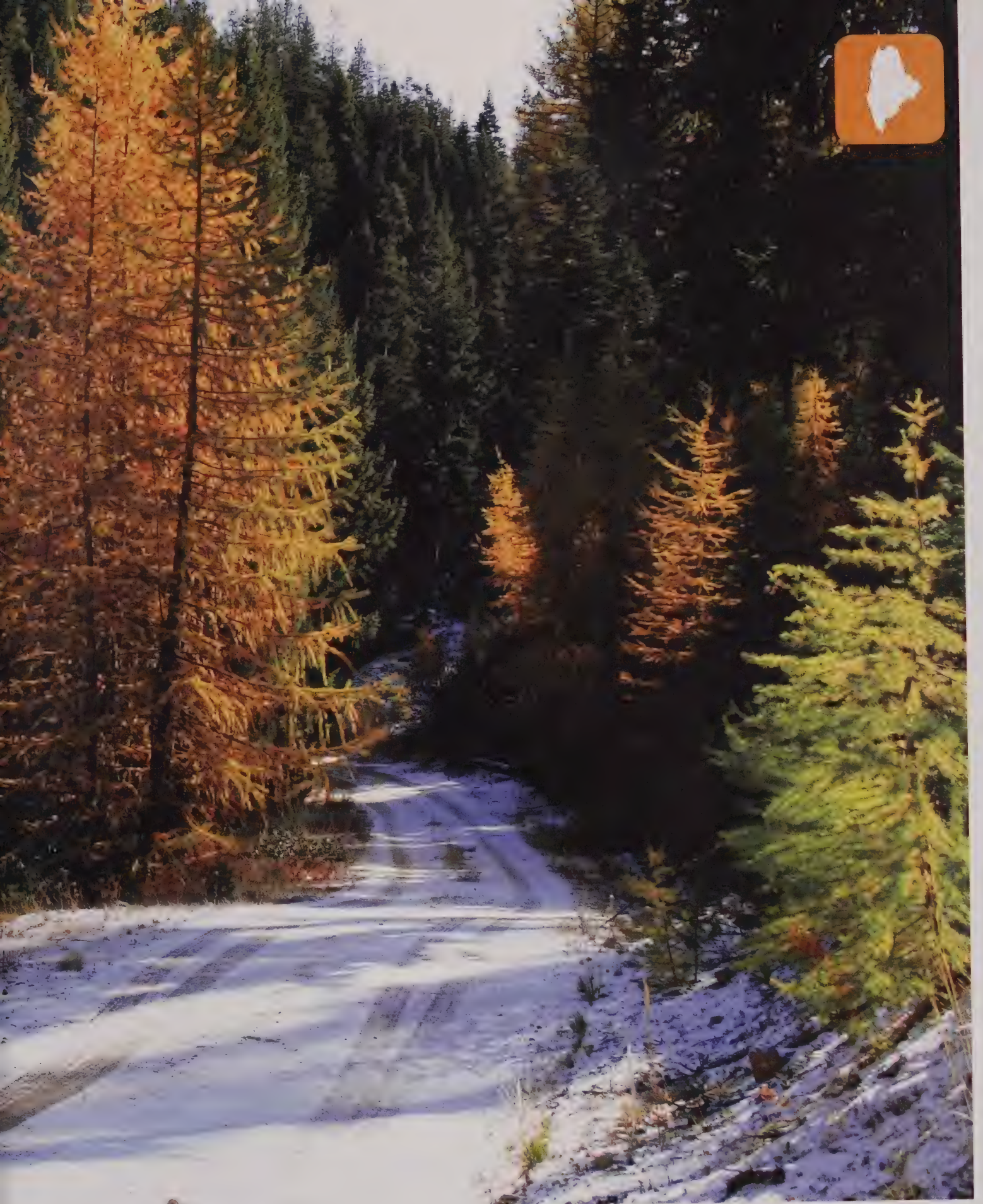
Jessica Cerretani is a Massachusetts-based health and medicine writer.



Shelter in Place

For the rural elderly, healthy aging often means remaining at home by Jake Miller

For some, home means the smell of the desert after a winter rain. For others, it might be the sound of spring peepers; the taste of the summer's first tomato, fresh from the garden and still warm from the sun; or the sight of gold-hued tamaracks through a frost-touched window. ■ More than one-quarter of the 50 million older adults in the United States live in rural areas or small towns, and for many of them, aging well means aging where the sights, sounds, and tastes of home are renewed with each new season—not locked in memories or frozen in photos that hang on walls far from the places they once called home.



I can't tell you how many people will say they will take whatever risks necessary—even dying, even spending hours on the floor without help—just to stay in their home,” says Louise Aronson '92, a professor of geriatrics at the University of California, San Francisco.

Unfortunately, that home may be hours away from a cardiac center, completely isolated from high-quality long-term care facilities, and bereft of local caregivers trained to aid the elderly.

As a demographic group, Aronson notes, older adults are the highest consumers of health care, the most likely to become hospitalized, the most likely to take medications and to have adverse drug reactions, and the most likely to be harmed by medical care.

Providing comprehensive, affordable care for this medically complex population, particularly in economically strapped rural areas, presents a tough challenge that clinical and policy experts say will require creative solutions. That challenge is compounded by the fact that as people age, they often face multiple chronic health problems without access to appropriate medical expertise and needed social supports. Older adults need access to acute and long-term health care, and some may also require help with transportation, nutrition, and managing the physical and cognitive demands of daily life. And they need these supports in ways that don't diminish their sense of self.

Hearing and Listening

In *The Heirs of General Practice*, the journalist John McPhee describes the complex interweaving of clinical, personal, cultural, political, and economic factors that affect the health of patients of several family medicine practitioners in rural Maine. Aronson says that the book provided her with insights into primary care that weren't always in medical textbooks, insights that also have relevance to her work in geriatrics. Perhaps most relevant is the importance of thinking about her patients as members of families and communities—and as individuals with histories and intensely personal visions of how they want to live their lives and what they do and don't want from medical care as they age.

This holistic way of thinking about health and wellness contrasts starkly with the mindset and funding streams that propel our health system, Aronson says. The current system, she says, too often focuses on diseases and organs instead of

on health and people, and it disproportionately values treating acute illnesses with high-tech interventions rather than implementing proven prevention strategies that promote health.

“We're so focused on biology we sometimes forget about caring and meaning,” she says. If treating patients with a particular class of drugs means that they lose their sense of balance and their ability to walk, it's better medicine to back off on dose or to try a different treatment so they can still exercise, work, and function in daily life rather than focus on getting their biomarkers into some textbook range of normal, Aronson adds. By the same token, if a patient chooses to stay in their rural home and live independently, it may be necessary to prioritize the older adult's sense of independence over family members' wishes for a safer environment and better proximity to medical care.

Gray Tide

“Over the next twenty years,” says Richard Frank, the Margaret T. Morris Professor of Health Economics in the Department of Health Care Policy at HMS, “the fastest growing sector of the U.S. population will be those age 80 and above.” Today, according to the U.S. Census Bureau, more than one in fifty rural residents is over the age of 80.

Caring for people in that age group is complicated, says Frank, who has worked on aging and disability in the U.S. Department of Health and Human Services, most recently from 2014 to 2016. As the department's assistant secretary for planning and evaluation, Frank was the principal advisor to the HHS secretary in areas such as policy coordination, legislation development, strategic planning, policy research, evaluation, and economic analysis.

Combined with the acute health problems that so many older adults struggle with are the chronic conditions that often come with aging. Some conditions have direct medical relevance, such as declines in strength, mobility, and cognitive function. But others, for example the impediments to safe driving that come with changes in hearing and visual acuity, can affect health indirectly: If there's no public transit where you live, driving is the only way you can get to a medical appointment.

Help Wanted

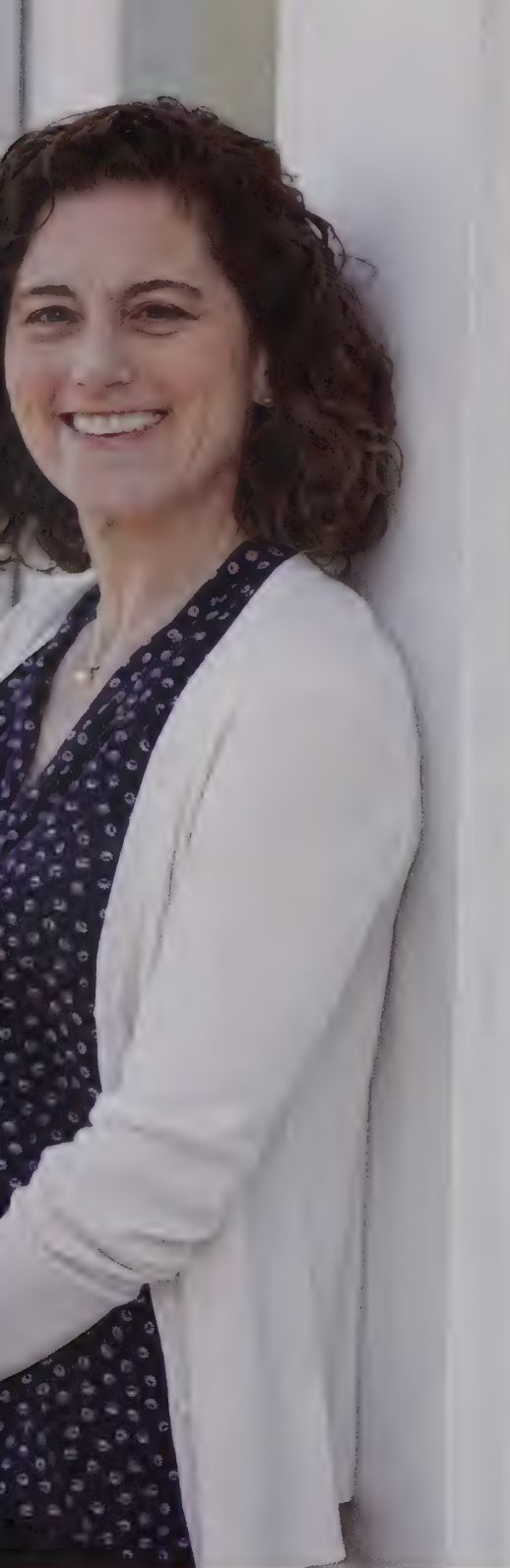
“We think of health care as being very local,” says David Grabowski, an HMS professor of health care policy who studies the economics



Louise Aronson

of aging and long-term care. “You tend to go to the nursing home that's up the street.”

In rural areas, there may be only one long-term care facility in a community or a single such facility serving a larger area, like a county. “That decreases the possibility there will be competitive forces to drive quality improvement,” says Grabowski. “If that facility is not providing high-quality care, there's nowhere else seniors can take their business.”



Richard Frank

And even if there were enough trained caregivers available, replacing long-term care facilities with home health aides presents other complications—distance, for one. Distance is such a recognized factor in providing care that some in the field have developed tools to track and reduce the time spent traveling from client to client.

Innovation Centers

A variety of technological and design advances have the potential to improve the lives and well-being of rural older adults. Aronson, who can almost hear Silicon Valley's hum from her office, points to two potential innovations: mobile robots with communications tools that let older adults video chat with health professionals, caregivers, and family; order groceries for delivery; or call for help if they fall, and driverless cars, which could help older adults living in remote areas overcome some of their transportation challenges.

Coming less from the pages of science fiction and more from the pages of medical journals is telemedicine, which Grabowski says might be a useful tool for clinical visits or for practitioners wishing to share expertise. Yet video conferences will not help with personal care—bathing or dressing, for instance—and even pared-down smartphones with preprogrammed options could prove challenging for older adults, especially patients with cognitive impairments, such as dementia.

Instead of trying to connect patients directly with remote experts, Grabowski says, it might be best to equip caregivers with simple tools that can help both parties make the most of their time together. One example, he says, might be found in a project he is now undertaking. The project asks home health aides to complete a checklist after each client visit. The caregivers use the list to monitor changes in a patient's physical or cognitive status—such as increased difficulty in walking—that may be clues to bigger problems. Flagging these little changes and initiating appropriate follow-up care early, rather than waiting until the condition requires clinical care, could improve a patient's well-being while also averting the need for more expensive care, Grabowski adds.

Local Perspectives

Whatever tools or aids are developed, they must be flexible enough to accommodate the profound differences in rural populations and the systems that serve their health care needs. There are, for instance, communities of Blacks that have worked the same land in Alabama for generations, while in Minnesota, there are communities of Laotian refugees who arrived within the past few decades. Established government systems, including the Department of Veterans Affairs and the Indian Health Service, can have parallels to other health systems but can also have points of divergence that make it difficult to transfer the innovations that work for one group to another group.

Even within a single ethnic group there can be vast cultural differences that must be considered when making clinical decisions. Consider the findings from a 2012 issue of the *Journal of Gerontological Nursing*. The researchers, three educators and health practitioners with personal and professional connections to native communities, found that discussions with elderly American Indians about moving to an assisted living facility needed to sensitively account for that elder's past. Was the person forced to attend boarding schools as a child? Because many such schools stripped children of their native identity, the prospect of moving to an institution might conjure painful memories—and sink any medical recommendation for advanced care.

There are also profound differences in what constitutes a rural community, from near-urban counties surrounding big cities to remote, sparsely populated near-wilderness areas whose residents may be more than 100

Although the U.S. Bureau of Labor Statistics indicates that the health care and social assistance sector now employs 12 percent of workers in this country, a percentage projected to reach nearly 14 percent by 2024, Grabowski says there remains a real shortage of caregivers and others who can provide support for older adults. To illustrate, he points to a recent survey of long-term care facilities in Wisconsin. It estimated there were 11,500 unfilled caregiver jobs in that state alone.



David Grabowski

miles from a hospital. The populations served can range from aging-in-place rural residents to snowbirds from northern cities who have chosen to spend their golden years in planned communities in warmer climes.

A variety of differences require a variety of solutions. Local initiatives, for example, can meet local needs, a line of thinking that underscores efforts ranging from having local tribal authorities coordinate care for their own older adults to creating the more than 600 Area Agencies on Aging. The latter were developed under the Older Americans Act of 1973 as the “on-the-ground organizations charged with helping vulnerable older adults live with independence and dignity in their homes and communities.”

Delivery Options

The landscape of health care for our aging population is no less complex than that for any other health care delivery system in the United States, with interconnecting public and private programs, providers, and institutions.

The Area Agencies on Aging coordinate a range of medical and social services important for the well-being of older adults in their designated communities, services such as

“We think of health care as being very local. You tend to go to the nursing home that’s up the street.”

education, home-delivered meals, transportation, and caregiver support. Many of these programs operate on limited budgets and could face cutbacks under proposed changes to social safety net programs such as the Patient Protection and Affordable Care Act.

According to Frank, other agencies outside HHS are exploring ways to provide older rural residents with the services they need to remain healthy. Working with the U.S. Department of Agriculture, some cooperative extension agents have begun incorporating outreach, monitoring, and education programs for older adults into their work. Veterans Affairs is developing Independence at Home, a program that would support in-home, long-term care to veterans for whom relocation to a facility is not a good option. Integrating these services and finding

new ways to deliver care outside the traditional health care system will be an important part of building more accessible and comprehensive health care for the elderly in the rural regions of this country, Frank says.

Time to Rethink

The lack of caregivers skilled in treating older patients and the potential complexity of the medical needs that people over the age of 65 face are “a crisis in our country,” says Lewis Lipsitz, an HMS professor of medicine at Beth Israel Deaconess Medical Center and director of the Hebrew SeniorLife Institute for Aging Research.

Lipsitz began his career as a clinician-scientist studying how the complex interactions of physiological systems promote healthy cardiovascular and mobility functions and how these systems lose complexity with aging and disease. More recently he has focused his research on multi-system interventions, such as tai chi, which can restore the complexity of these systems and, in doing so, improve physical function. According to Lipsitz, this concept of healthy complexity may also apply to health care systems.

Because interactions with geriatric experts are rare and the care of elderly patients is complex, Lipsitz has helped pilot two models that bring geriatric expertise to nursing homes: a demonstration project supporting on-site “enhanced care and coordination providers” and a remote case-based video consultation program called ECHO-AGE. In a 2016 presentation at Brown University, Lipsitz reported that these models have been shown, respectively, to prevent avoidable hospitalizations and lower the cost of care and to reduce the use of physical restraints and antipsychotics.

Programs like these, along with various state and federal training programs and fellowships, can provide a foundation of geriatric expertise for physicians and other caregivers committed to working with rural elderly patients. Aronson notes that it’s vital for the medical community to radically rethink medical education and incorporate in it an understanding of the processes of aging and its biosocial effects. But a move to reconceptualize aging in our society should not only fall to clinicians. That effort, she points out, needs to be addressed by biomedical researchers, architects, product designers, community planners, policymakers, and other professionals who can help remake the way we serve people of all ages, wherever they live. ■

Jake Miller is a science writer in the HMS Office of Communications and External Relations.

FROM THE COLLECTIONS AT HARVARD MEDICAL SCHOOL



A gym bag, a designer handbag, a doctor's bag—each tells you something about the person carrying it.

In the nineteenth century, the majority of this country's population lived in small towns and rural areas. Even cities had far-flung neighborhoods. Whatever the address, when people fell ill or were injured, physicians often traveled to

treat them with supplies carried in that doctor's bag.

William Henry Porter came by medicine almost osmotically—both his father, Vine Porter, and his older brother, Winslow Burroughs Porter, practiced the medical arts in and around Surry, New Hampshire.

William attended lectures at HMS in 1851-1852, received his

medical degree from Worcester Medical Institution in 1853, and then apprenticed in Winslow's practice in Alstead, New Hampshire, near where the brothers had grown up.

William eventually married, moved to Surry, and established his own practice there in 1854. He was far from just the local doctor, however. Deeply involved in the community, he served as town clerk, treasurer, the town representative to the state General Court, the postmaster, a school board member, a trustee of the local library, and a member of the Surry Grange.

If the bag doesn't make the doc, it does reveal, to a degree, the type of doctor he was and the medical care he customarily provided his patients.

Judging from its homemade lining and utilitarian mien, William's rectangular bag probably was a repurposed suitcase. Contained inside are tooth keys for extractions, gynecological devices, forceps, splints, and medicines; notably absent are surgical implements.

Judging by these contents, William likely delivered babies, terminated life-threatening pregnancies, set broken bones, tried to bring fevers down, and treated diarrhea with morphine or vomiting with anti-emetics.

William's immersion in the life of Surry likely served him well as he cared for his friends and neighbors in town and surrounding areas, where he enjoyed a successful practice for many years. Today, telemedicine can help doctors reach people in rural areas or those who cannot leave their homes. And the doctor's bag is still handheld—but it needs to be charged.

—Susan Karcz



Why jazz is my religion and Wally's is my temple by Cuthbert Simpkins

COLTRANE

AND ME

IT WAS 1971, and nine years had passed since my family had become refugees in our own country, forced from Shreveport, Louisiana, following the bombing of our home by white supremacists. The terrorists had hoped to crush my parents' efforts to secure the vote for Blacks in the United States. But they failed: the Voting Rights Act had become the law of the land, my family was intact and thriving in Queens, New York, and I, a young man who had been denied use of the Shreveport public library because of my skin color, had earned my baccalaureate degree in chemistry at Amherst College and completed my first two years at HMS. ■ I also was about to begin a one-year leave of absence to write a biography of the musician-composer John Coltrane.



A LOOK BACK: This photo of the author appeared on the dust jacket of the his Coltrane biography.

I had begun work on the biography during my senior year at Amherst. One night after working hard deriving equations for my honors chemistry thesis, I listened to Coltrane's "Manifestation." I had listened to Coltrane's music since high school—his work in particular and jazz in general were the vehicles through which I explored and discovered my inner self. In part, this discovery was enhanced because I have a synesthetic response to music: my brain interprets each note as both sound and color. But I am also

drawn to jazz because it abstracts music to its basic elements—chord sequence, modes, or rhythms—and then uses those elements as a platform from which a talented improviser can derive limitless ideas and emotions.

That night in Amherst, "Manifestation" caused me to shake uncontrollably and to see multicolored particles moving randomly in my mind's eye. The next morning I declared to myself that I would write a book about John Coltrane. I wanted

others to know of the wonderful discoveries Coltrane had made in the emotional universe and realized through his music.

When it became clear that the only way I could complete the book was to spend extended time away from my classes, I talked with my advisor at HMS, S. James Adelstein '53. We settled on my asking for a leave of absence, for this would allow me to officially remain a medical student and retain my medical draft deferment: It was that deferment and a high lottery number that had kept me from the front lines in Vietnam.

I didn't learn about the controversy that my request stirred up until many years later. One or more of the members of the Board of Advisors worried that I would never return to medical school. But Dr. Adelstein assured them that I would return and, further, that I would do well when I did. That's exactly what happened.

Blue Train

At that time, I was living in Boston's South End. That was well before the area had become gentrified. My apartment was in a building owned by a Black man who also worked as an electrician. Although rents then were cheap in that area, ours were cheaper—Mr. Keel had worked things out so that our electricity was free.

Almost every day I would walk the neighborhood, wearing a djellaba or dashiki and playing Coltrane's "Moment's Notice" on my recorder. Over time, I got to know some of my neighbors—Freddie, the trumpet player; Nineta, the female saxophone player; Coldcut, the building supervisor and numbers runner; Tiger, the former boxer who lost his eye in a fight with Sugar Ray Robinson and had a boxing school in the neighborhood; and Killer. I never asked Killer what he did. In the building next door lived my dear friend George Turner, a carpenter who worked for Harvard.

Everyone had heard I was a medical student, but most didn't believe it. After all,

a lot of the people who lived in the neighborhood pretended to be a lot of things. But George knew I was in medical school, and so did Bobby Neloms. I had met Bobby, who had attended Berklee College of Music, at Wally's Cafe Jazz Club on Massachusetts Avenue. He played organ there. Now those who know jazz, and have been around Boston, know Wally's is the place to hear music. It was and still is, a landmark for anyone who admires jazz. For me, it became a home away from home.

Bobby and I often would get together in my apartment and listen to jazz. I remember one visit in particular. I had been working on the book quite a bit and asked Bobby to read the manuscript. We were listening to Coltrane, when Bobby suddenly jumped up, threw the manuscript across the room, and angrily shouted, "This reads like *Reader's Digest*!"

I was stunned. I wanted my book to be Coltrane, to breathe and pulsate with movement and life. I wanted it to show how he came to express his creative genius and to show the struggles he had faced to create his music. I wanted to show how he became what he sought to be: a force for good. So when Bobby delivered his verdict I realized that I needed to forget about what critics might think, forget about offending people, and stay true to Coltrane's story.

Alabama

I was born in Chicago, my mother's hometown. My mother held a degree in sociology from Tennessee State University in Nashville and had the chance to work with W.E.B. DuBois, but she got married and had me instead. My brother and sisters followed; my mother remained a homemaker, but also helped my father with his work. My father was a dentist—he graduated from the Meharry Medical College School of Dentistry in Nashville—and had a practice in Shreveport. He also was a leader in the United Christian Movement in Shreveport and a fourth vice-president and founding member of the Southern Christian Leadership Conference.

Although the United Christian Movement was composed mostly of ministers, my father was the president and the only layperson in leadership. My mother led the student arm of the organization, held voter registration classes, and taught people how to vote. We had leaders of the civil rights movement come by our home: Reverend King, Reverend Abernathy, Ella Baker. I got to see all of these great people doing something they believed

in without any financial incentive or promise of success.

This activity had a cost, however. I grew up knowing that the phone in our home was tapped, and that my parents regularly received threatening calls. It wasn't unusual for the Shreveport police to come by our house looking for affidavits that had been gathered from local residents for submission to the U.S. Commission on Civil Rights in Washington, DC.

I also remember each of my parents being arrested. During one of the times my father was taken to the police station, the police bargained with him—stop the civil rights work and you and your family can do "anything the whites can do" in Shreveport. He refused and continued the work.

A time my mother was arrested occurred when I was about eight years old. She was taking me and other Boy Scouts on a field trip. We went on a city trolley, and my mother and I sat up front. A white woman objected, my mother refused to move, and the driver called the police. Before the police came for her, however, she arranged for us boys to be driven home; she didn't want us to be humiliated. She didn't want our spirits to be broken.

That's what was important to my parents—they wanted to protect our spirit. My father encouraged my interest in science and had designed a laboratory, complete with telescope and a short-wave radio, for me in our house that was later bombed. And my mother always reminded me that my integrity was worth more than anything else.

I wanted my book to be Coltrane, to breathe and pulsate with movement and life. I wanted it to show how he came to express his creative genius and to show the struggles he had faced to create his music.

"You're a citizen of the world," she would tell me, "you are not limited by America."

Their words made me realize that if I wanted to do something, I could do it. So when I decided to write a book about Coltrane, even though I'd never written much of anything, it didn't occur to me at all that I couldn't do it.

Wise One

I conducted my first interview for the book in the summer after graduating from Amherst. I had been listening carefully to Coltrane's music and reading all the liner notes I could find, but I knew I needed to start talking to people who had been part of Coltrane's life.

It turned out that Naima Coltrane, Coltrane's first wife, had a dashiki shop up the street from my father's dental office in Queens. I wanted to talk with her but was shy. I kept talking about it but also putting it off. Finally, my father said, "What's wrong with you?" and challenged me to meet with her. I had no choice; I went to her shop.

She was so kind and welcoming. Her manner was that of a person who was in control of her thoughts—and interested in yours. I explained my intention to write a biography of her former husband; she welcomed the idea.

From Naima I received suggestions of people I should interview and advice on how to approach the family. It was a close-knit family, she said, and protective, so I would need to navigate carefully. I ended up spending a lot of time with her and her daughter at their home. Years later, when she had read the finished book, I talked with her and asked, "Naima, is this John?" She smiled and nodded yes.

I was equally welcomed by the jazz artists who had performed with or knew Coltrane: Pharoah Sanders, Yusef Lateef, Max Roach, Gary Bartz, Jimmy Garrison, Elvin Jones, and Rahsaan Roland Kirk, to name a few. I remember I became dumbstruck when I approached McCoy Tyner. Tyner had been peeling an orange, so when I just stood there, he asked me, "Would you like a piece?" I relaxed and we talked.

I was also nervous about talking with Thelonious Sphere Monk. When I caught up with him he was in the back of the kitchen in the Village Vanguard, a Manhattan jazz club, holding his drink. He turned, looked at me, and said "Uhhh?" I immediately forgot every question I was going to ask.

I realized there are no barriers between human expression and human knowledge. Concepts are interchangeable and not limited by the discipline in which they appear.

Finally I came up with, “Why did you have Coltrane in the band?” At the top of his voice he shouted, “He could play the horn, he could play the horn, he could play the horn!”

My interview with Monk then ended.

Impressions

As I delved further into Coltrane’s life, I learned that one often would find him at 3 a.m. in his hotel room with twenty or so books open on the floor. The books would be about music, mathematics, physics, history, religion, and any other subject that he felt related to music. He would draw abstract patterns and relate them to the music. I also learned he was uncompromising in his pursuit of truth through music. Despite the demands of record companies, the outcries of critics, and sometimes the disapproval of audiences, he remained focused and undaunted. My mother’s admonition, “Always maintain your integrity!” echoed in my head.

Coltrane became the role model for anything I did. When I studied linear algebra, I saw the matrix basis to be the same as a chord progression that determined the broad outlines of improvisation. I could see pseudo randomness in the patterns of light that I saw when listening to “Manifestation.” When I would see a patient incapacitated by stroke, I would think of Coltrane’s “After the Rain.” I realized there are no barriers between human expression and human knowledge. Concepts are interchangeable and not limited by the discipline in which they appear.



Cuthbert Simpkins

Dial Africa

I was still writing my book when I returned to HMS and started seeing patients. I finished the first draft and submitted it to Emerson Hall, a Black-owned publishing house in New York City. A year later, when we were about to publish, I found they had rewritten my book, removing anything that might be politically provocative. I was angry and began working to get my manuscript back. Fortunately, I was able to reconnect with Harold Wade Jr., a friend

from Amherst who had just graduated from Harvard Law School. His advice: “Threaten to sue the cat.”

So I did.

I got my book back but now needed a new publisher. I tried other large publishing houses but, although there was interest, I worried about having my work changed. I decided to self-publish under the name Herndon House. Herndon was my mother’s name before she married.

In 1975, I succeeded in publishing my book. It garnered favorable reviews in the press and was enthusiastically received by the music and literary communities; there was even a book party and benefit for the Schomburg Collection of Black History and Literature at the New Lafayette Theater in Harlem.

Ultimately, however, working out distribution and reprint details became too much—I had to focus on my surgical residency. The book did not get broadly distributed, and eventually went out of print. I do, however, retain the rights and still hope to again publish the biography, especially given recent interest in it.

Giant Steps

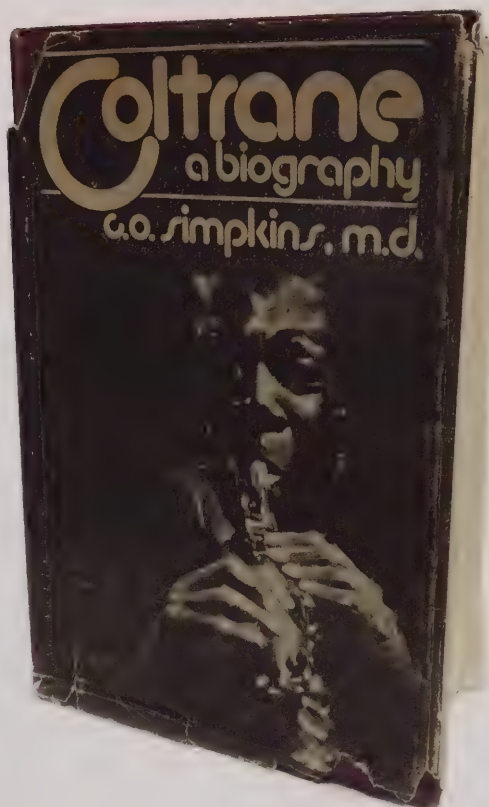
Like Coltrane, I have come to feel that to live is to risk. After a long career as a trauma surgeon, managing complex injuries such as gunshot wounds of the heart or lacerations of the liver or vena cava, I retired and now just do critical care. I also retired so that I could care for my ailing mother and focus on building the biotechnology company I formed to commercialize patents that I received for a new circulatory support fluid.

The fluid is based on the salutary biophysical properties of phospholipid nanoparticles. In these nanoparticles, I see a connection between the randomly moving colored particles conjured by my brain after hearing “Manifestation” and the Brownian motion that keeps the nanoparticles from settling out, making the fluid more effective.

Although my wife, Diane, and I are working hard to make this company successful, we have already achieved our first victory: My goal was to develop a potential solution to an important medical problem, and I’ve done that. Patients who once died from complications associated with volume replacement fluids they received after an otherwise successful surgery may now be able to live.

I’m prepared to go on and live whatever is left of my life, guided by the chord changes and rhythms of my soul. ■

Cuthbert Simpkins '73 is a retired trauma surgeon. He has long been active in trauma prevention programs. At the University of Maryland School of Medicine, he designed and initiated a violence prevention program that has proven effective in preventing recurrent incidents of trauma to patients who were victims of interpersonal violence. He formed his company, Vivacelle Bio, Inc., in 2013.



A Young Man's Petition

by S. James Adelstein

During the early 1970s, I would serve each year as a student advisor to two or three students, helping them choose their courses. One of the students I was assigned was Cuthbert Simpkins '73, a Black student who had attended Amherst College, where he had concentrated in chemistry as a premed. While at Amherst, Tuffy, as he was known to just about everyone, had also begun to write a biography of John Coltrane, the jazz saxophonist and composer.

At that time, the medical student curriculum at HMS had few required courses. Each student, working with his or her faculty advisor, would create a course of study composed mostly of traditional clinical clerkships and electives. In all honesty, the course dance cards were remarkably similar to each other, and, for Tuffy's first two years, his course choices were nothing out of

the ordinary. I was therefore surprised when he announced, sometime in 1970 or 1971, that he wished to take a year off to continue writing his biography of Coltrane. It was necessary, he said, for in addition to his lifelong interest in jazz, he had made a promise to Coltrane's widow that he would continue his biography of this highly original musician.

Had Tuffy asked to take a year off to do biomedical research there would have been no issue. But I knew this request would be a hard sell to the Board of Advisors. The advisors would consider his petition to be irrelevant to his professional development. Furthermore, they would not want to risk losing such an academically promising student. In addition, Tuffy was a member of a vanguard cohort. In the 1970s, the School, spurred by the assassination of Martin Luther King Jr., and by a petition from a group that

included child psychiatrist and social medicine advocate Leon Eisenberg and HMS neurobiologists David Potter and Edwin Furshpan, had taken action to make the HMS student body more diverse.

But Tuffy persuaded me that this was a serious intent of his and not a prelude to dropping out. To help his cause, I joined with Hermann Lisco in making his case to the Board. Hermann was an associate dean for student affairs and a much-loved student advocate. He was also a German-born intellectual who thought it entirely reasonable that a medical student would write a musician's biography. Ultimately, yet with some skepticism, the Board acceded to Tuffy's petition.

Although I had asked Tuffy to keep me informed of his progress, we each became busy, and a year slipped by. Then, some time in June before he was slated to resume his studies, I received a note from him telling me he was coming back to HMS as planned. And so he did. The Coltrane biography, published two years later, brought a musical genius to life while also bringing acclaim to its young physician-author.

S. James Adelstein '53, the Paul C. Cabot Professor of Medical Biophysics Emeritus and the HMS Daniel C. Tosteson University Professor in the Department of Radiology, was the HMS executive dean for academic programs from 1978 to 1997.

FIVE QUESTIONS

FOR PATRICK LEE ON BRINGING MORE RESPECT TO HEALTH CARE



You've written that the quote "the secret of quality is love" has meaning for you. Can you explain why?

It's a quote from Avedis Donabedian, who many consider the founder of quality improvement and outcomes research in health care. And it's an idea that guides me in everything I do. When we take the time to understand what matters to each of us, why we care about each other, and why we care about this problem, we strengthen trust and shared purpose. Teams learn and perform much better under these conditions, and quality improves.

You talk often about fostering respect and dignity in health care. How do you put this into practice?

At our clinic in Lynn, we follow the tenet that we're here to increase the dignity and respect in each person's life. I learned this way of working in my first job out of residency, with Partners In Health in Rwanda. It's the language I've tried to use in every job I've had.

If I want to make a difference in the justice and health that people experience through the care they receive, then this is the most effective way I know of to do that.

To what do you credit your ability, your openness to absorb this kind of approach?

My mom, in particular, allowed me to understand that no matter what, she would be there for me if I needed her. I understood, at a deeper level than language, that I was worthy of love.

Both my mom's parents died from cancer. My grandmother chose hospice care rather than dying in a hospital, but she still endured great suffering. When she passed, my mom said, "If you do go into medicine, I want you to think about dignity, because I'm not sure that the health system has fully understood that yet."

Affiliate, Department of Global Health and Social Medicine, Harvard Medical School

Assistant Professor of Medicine, Beth Israel Deaconess Medical Center

Chief Performance Improvement Officer, Lynn Community Health Center, Lynn, Massachusetts

You've talked about "purpose power." How does this work in practice?

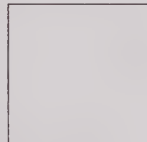
In many of our workplaces there is a deep river of purpose that we don't take the time to recognize or harness.

In Lynn, we spend three out of four staff meetings doing workflow design and development. We're in what we call systole, when the heart squeezes and pushes blood through the body. In the fourth meeting, we get to diastole, where the heart relaxes and nourishes itself. We share meaningful stories from our work and take time to learn from our experience. I believe diastole is the most important meeting we have.

How do you think about your work within the current health care landscape in our country?

Poor and disabled people have been left behind in communities across the country, accessing care too late when disease is already advanced, often in emergency rooms and hospitals, and at enormous cost. We've known for decades that community health centers are an effective solution to this problem. That's why they have consistently had strong bipartisan support—it's both the right and practical thing to do.

—Susan Karcz



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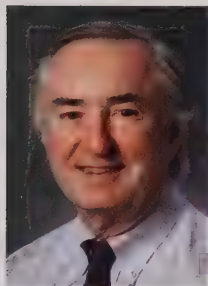
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THE COMMUNITY OF HARVARD MEDICAL SCHOOL ALUMNI

President's Report



Spring has arrived and departed several times during the past several weeks, teasing us as we anxiously await the

warmth that brings Boston back to life. Graduation season is behind us, as are the reunions that brought together cherished friends even as they reminded us of how fleeting the years can be.

When the Council met in March, we tackled a full agenda that began with an update on the new curriculum from Ed Hundert '84, HMS dean for medical education, who described the remarkable software tools for everything from storing educational materials to measuring use, and the mechanisms for encouraging and acting upon student feedback. Fidencio Saldaña '01, HMS dean for students, reported on new student advising efforts before rushing to monitor the excitement of Match Day for the HMS Class of 2017. Joan Reede, HMS dean for diversity and community partnership, shared her passion and optimism in describing her office's programs while underscoring the deep commitment to increased diversity that she shares with Dean George Q. Daley '91. Reede emphasized the critical need for funding to sustain these programs.

Emily Oken '95 updated the Council on the Welcome to Your City Project, initiated by fellow Council member Carolyn Walsh '09. This program seeks to pair HMS alumni in cities beyond Boston with graduating alumni beginning residencies in new communities. To further this



program, the Council agreed to contact alumni representatives at the top five most commonly matched medical centers and encourage them to reach out to the new residents in their midst.

Ann Marie Menting, *Harvard Medicine* editor, and Susan Rice, senior director of alumni engagement, presented data that plotted the diminishing number of submissions to Class Notes in the magazine, data that generated further exploration of new approaches to involve alumni in the magazine. Council members agreed on a new effort that would invite alumni to respond to questions that would allow them to reflect on their time

as students or on their profession as a whole.

A presentation by members of the Office of Alumni Affairs and Development touched on three areas: plans for the upcoming Council elections, reunion planning, and the new Meet the Dean event series. This letter will reach you after the Council elections and the vote on proposed changes to the Alumni Association's constitution have taken place. To review the results, visit hms.harvard.edu/about-hms/alumni/getting-involved/alumni-council/elections. The first Meet the Dean event occurred in Boston in early May; subsequent events are scheduled

in New York City (September 13), Washington, DC (September 18), San Francisco (October 10), Los Angeles (October 11), and Philadelphia (November 1).

The Council meeting on May 23 and 24 was my last in the role of president. This has been a very special year for me and I cannot thank you enough for your support, devotion, and friendship during this year of transition. I am beyond excited as we welcome Dean Daley and look forward to a new era at HMS.

James O'Connell '82 is an assistant professor of medicine at Massachusetts General Hospital and president of Boston Health Care for the Homeless.

CONNECT THE DOCS

THE COMMUNITY OF HARVARD MEDICAL SCHOOL ALUMNI

ON TOUR

Dean George Q. Daley greets alumni and friends at the first Meet the Dean event

"IMAGINE YOU HAD A CONSTRUCTION set and could build the perfect dean for Harvard Medical School. I think if you played around with that set, every one of you would come up with George Daley."

With that introduction, Michael Rosenblatt '73, president-elect of the School's Alumni Council, chief medical officer at Flagship Ventures in Cambridge, Massachusetts, and former dean of Tufts University School of Medicine, welcomed George Q. Daley '91 to speak to alumni, faculty, and friends attending the first of six Meet the Dean events.

The interstate tour will allow the new dean to meet with and present his vision for HMS to the extended Harvard community. Additional gatherings are scheduled in Los Angeles, New York, Philadelphia, San Francisco, and Washington, DC.

"We're on the brink of a sweeping transformation of the human condition," Daley told the gathered crowd. "Medical breakthroughs in the next fifty years will dwarf those of the past one thousand."

Forging the path to the future of medicine will require embracing innovation in research and therapeutics, committing to campus revitalization, and expanding access to medical education, Daley said.

Innovation, he added, includes translating HMS laboratory discoveries into new treatments and cures for diseases, whether widespread or rare, local or global.

Seizing the future of science requires rethinking how research is conducted, from recognizing the value of technologies such as bioinformatics and cryo-electron microscopy to forming new collaborations across the School and its affiliates, within the thriving Boston biotechnology and pharmaceutical communities, and with other industries and institutions in the United States and abroad, Daley said.

To ensure that HMS continues to cultivate future generations of leaders in research and health care delivery, Daley emphasized the need to foster diversity and free exchange of ideas and to make medical education as debt-free as possible. One of the goals he described is to double the number of fully funded MD/PhD students accepted to the School.

"Students entering HMS today bring with them a fierce passion to both heal and innovate," Daley said. "If we can couple that idealism to today's cutting-edge technologies, then I believe the work we are doing will revolutionize the quality and richness of human life."

—Stephanie Dutchen





Attendees at the Boston Meet the Dean event included alumni, current students, members of the Ezekiel Hersey Council, and other friends of HMS.

Who Was Your Dean?

At Boston's Meet the Dean event, several alumni were asked for their recollections of the person who served as dean of HMS while they were students. Here are the decanal stories those alumni shared.

My dean was George Packer Berry.

I felt close to the dean and occasionally talked with him. It was a smaller world then, there weren't so many in the administration. You felt related to everybody.

Firmon Hardenbergh '56

My dean was Daniel Tosteson '48.

We didn't have much contact with Dr. Tosteson, but we did see a lot of Dr. Daniel Federman '53, the dean for students. Dr. Federman was very dynamic and brilliant.

I recently had a chance to recall my student days, for I attended to my daughter's white coat ceremony. When I was a student, there was no White Coat Day. What happened was that in your second or third year you would turn up at a hospital—in my case, it was Massachusetts General Hospital—and you would be sent to the laundry in the basement. Someone there would say, "You look like a medium. Here, put this on." And that was it. You had a white coat!

Mark McMahon '86

My dean was George Packer Berry.

On our first day of medical school, we sat in one of those old auditoriums and Dr. Berry said, "Gentleman and ladies (there were only seven women), what we are about to teach you, half of it is wrong and half of it is right. Our problem is, we don't know which half is which." And he was right! I think that, except for anatomy, everything else has changed since I was in medical school.

Newton Hyslop '61

My dean was Daniel Tosteson.

I knew Dan very well. I came for my admission interview in 1977, which was exactly when he started as dean, and I left HMS the same day he retired. I moved to the University of Rochester, where I served as dean of the School of Medicine and Dentistry. He was my boss during the seven years I served as the HMS associate dean for student affairs. It's been wonderful to be back these past 10 years, but I always remember that my first "tour of duty" at HMS exactly overlapped with Dan's 20 years of being dean.

CONNECT THE DOCS

THE COMMUNITY OF HARVARD MEDICAL SCHOOL ALUMNI

Dan had a great vision for both science and education—a lot like Dean Daley. He was a basic scientist and a teacher who was passionate about education and access to medical education. And he was a terrific fund-raiser. The School's science enterprise, educational programs, and endowment all ballooned during his tenure as dean.

I know from my roles as the School's dean for students and now dean for medical education that the relationship between the HMS dean and our medical students is an important one. Dean Daley is a great listener. Every time we meet, he's looking for more opportunities to interact with students. He loves forming relationships with the students and knows many of them already through interactions he's had with them in the classroom, in his laboratory, and through his diversity task force and the social justice coalition. We are so lucky to have him as our dean!

Edward Hundert '84

My dean was Robert Ebert.

I remember Dr. Ebert. He was an inspirational leader. I thought he promoted respect for the practice of medicine, not just for medical science.

Steven Kanner '69

My dean was Daniel Tosteson.

I remember Dr. Tosteson as a smart guy, but a boring lecturer. His red blood cell lecture put us all to sleep!

Eliza Menninger '87

My dean was Charles Sidney Burwell.

I don't have a strong memory of Dean Burwell and don't think I was strongly influenced by him. But I was a classmate of Dan Tosteson; he was a good friend of mine.

John Stoeckle '47

My dean was Daniel Tosteson.

My only recollection of Dr. Tosteson was that he was a very bright, talented leader who had an appropriate but dry sense of humor.

David Kieff '92

My dean was George Packer Berry.

At the opening session for our class, Herrman Blumgart '21 talked to us, but I have no recollection of Dr. Berry addressing our class nor do I think I saw him. We saw Joseph Gardella, the dean for students, and Noreen Kohler, who was the registrar. Building A, which is now Gordon Hall, was known to us primarily as the medical library, which was on the second floor. That was about the only thing we went to Building A for. The faculty room was there, too—you could fit the entire faculty into that one room. On the top floor was the Warren Museum.

A.W. Karchmer '64

My dean was Robert Ebert.

I remember Dean Ebert very well even though it was unusual for medical students to have any contact with the dean, especially in those days. It was just after the Vietnam War and the National Institutes of Health had instituted a program designed to get physicians to commit to doing research at the NIH—the "doctor draft" was over but the need remained. The program would pay your medical school tuition and support your research, followed by your undertaking research at NIH. Participation in the program would count as your military service.

A number of us signed up for the program—and none of us got in. So we brought this to the attention of Dean Ebert. He called the head of NIH and said, "I don't understand. You have this great program, we've got these great students, how is it that not one of them got into this great program? It doesn't seem possible." The NIH director said he'd look into it and get back to us.

It turns out that somehow our applications had gotten lost; those were paper applications. So Dean Ebert called together all of the students who had applied and arranged for a call with the head of the NIH. He got on the phone, told the director about each of us and, by the end of that call, we were all in the program.

As fate would have it, years later during my tenure at HMS I was named the Robert H. Ebert Professor of Molecular Medicine at Harvard Medical School.

I was the dean of Tufts University School of Medicine for seven years, and I know that being dean is a really hard job. I don't think anyone knows how hard the job will be for George Daley. We really need to thank him for taking it

on. This is a great school and it requires great leadership to keep it going. But in addition to providing great leadership, George will need to use the bully pulpit that his position offers to be a spokesperson for U.S. medicine and science on a national and an international level.

Michael Rosenblatt '73

My dean was Daniel Tosteson.

I remember we poked fun at him in our Second Year Show. We had a character named Dean ToasterHead.

Samir Shah '92

My dean was Charles Sidney Burwell.

I think I was more impressed with Dean Daley today than I was by my dean.

My grandfather was a country doctor and I have a textbook of his, from 1902, that says that to operate in the heart was a fatal mistake. I've been a cardiac surgeon my entire career!

Charles Lasley '47

My dean was Daniel Tosteson.

As medical students, we felt pretty distant from the dean. I remember more about Dr. Federman. He was the dean for students for years and years and had a huge impact on me as a student.

Megan Murray '90

My dean was George Packer Berry.

I never talked with Dr. Berry, but may owe my career in medicine to Kendall Emerson Jr. '33, who was his dean for admissions. When I was a senior at Radcliffe, Dr. Emerson came to a premed society meeting. It was the first such meeting I had attended, for I had planned to enter graduate school in biochemistry. He was there to encourage more women to apply to HMS. He said HMS was looking not only for women with strong science records but also for women who could bring the perspectives of wives and mothers to the field of medicine. I was astonished! The application deadline had passed, and I had taken the GRE but not the MCAT, but I called HMS anyway. I was admitted without the MCAT, but was told I would need to take the test in the spring. The day before I was to take the MCAT I was rushed into surgery with acute appendicitis. I never took the test.

Eleanor Shore '55



Irene Zhang

The Chance for Change

Albright symposium highlights new research, leadership vision

HMS STUDENTS “are going to be our game changers,” said Tenley Albright ’61, as she announced the winner of the 2017 Hollis L. Albright, MD ’31 Scholar Award—fourth-year HMS student Irene Zhang—at the Hollis L. Albright, MD ’31 Symposium, held in March.

In accepting the honor, Zhang said, “It is a great privilege to be able to come into patients’ lives at a time when they are most ill and vulnerable and do something with our hands and minds that allows them hope and a chance to change their trajectory for the better.”

The faculty member who nominated Zhang, Anthony D’Amico, an HMS professor of radiation oncology at Brigham and Women’s Hospital and the advisory dean of the Oliver Wendell Holmes Society, of which Zhang is a member, praised Zhang’s intellect, selflessness, and dedication to her area of academic interest, molecular oncology.

Tenley Albright established the Albright symposium with her brother, Nile, in honor of their father, a surgeon who dedicated his life to patient care and student mentorship.

The 16th annual symposium, “The Power and Promise of Harvard Medicine,” featured keynote speeches from HMS Dean George Q. Daley ’91, Dana-Farber Cancer Institute President and CEO Laurie Glimcher ’76, and Vertex Pharmaceuticals Chief Scientific Officer David Altshuler ’90.

The program focused on a few recent inspiring developments in the HMS community, including cancer immunotherapy and personalized genomic medicine.

Daley shared his vision for building on the School’s dedication to excellence in research, education, and health care delivery.

“Some revolutionary technologies exist now,” he said. “When coupled with the passion and idealism of our students, trainees, and faculty, these tools are allowing Harvard Medical School to change the world.”

Altshuler described how researchers are entering a long-anticipated era of developing personalized medicine for genetic diseases.

“No one could imagine a protein that would fix a molecular defect” like the one that causes cystic fibrosis symptoms, Altshuler said, until someone tried it and proved it could work.

Achieving the vision of translating gene discoveries into disease treatments will continue to require new types of chemistry to target molecules that scientists currently deem “undruggable,” added Altshuler.

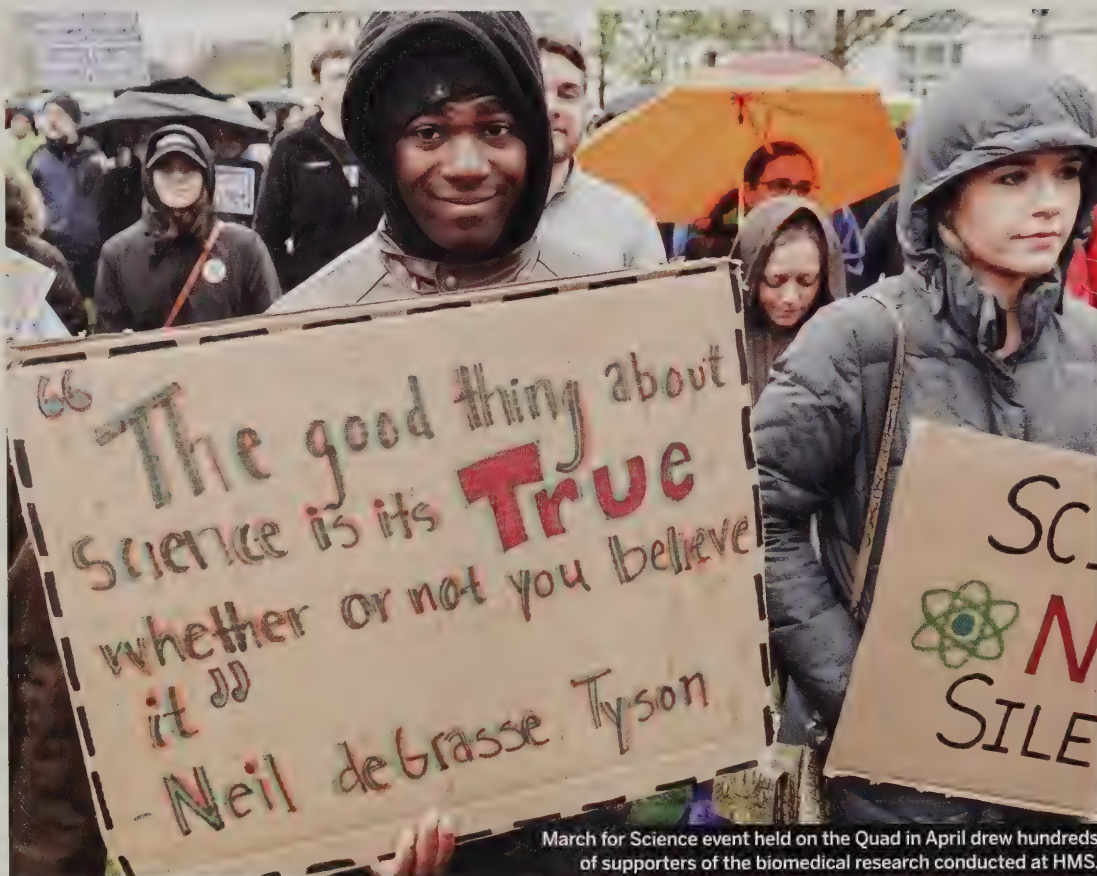
Glimcher expanded on the translation theme. “It’s a transformational time for cancer care and treatment,” she said. According to Glimcher, excitement is running high because cancer immunotherapy has finally become a reality a century after it was first conceived. Unlike traditional cancer treatments, cancer immunotherapy prods a patient’s immune system to turn against cancer cells.

Cancer immunotherapies have already been game changers for several types of cancer, and those therapies, said Glimcher, are “just the beginning.”

—Stephanie Dutchen

CLASS NOTES

NEWS FROM ALUMNI



What Is Your Favorite Vanderbilt Hall Memory?

Surely you have one or perhaps several memories of life in Vanderbilt Hall when you were a student. The editors of your alumni magazine would like to share your stories with your fellow alumni. To help us do so, the Autumn 2017 issue of *Harvard Medicine* magazine will introduce a new section designed specifically to capture the voices, memories, and insights of HMS alumni. Dubbed "Rounds," this section will carry alumni responses to a specific question, posed in each issue as well as in materials sent to you by the Alumni Advancement and Development Office (AAD).

This new section resulted from the realization that most alumni are sharing personal updates on social media instead of through the Class Notes format. So, to continue to capture and celebrate alumni voices, School history, and intergenerational exchange, AAD, the Alumni Council, and the editor of *Harvard Medicine* developed this section.

We invite you to share your Vanderbilt Hall memories and respond to other "Rounds" questions online at <https://hms.harvard.edu/rounds>. You may also email us at hmsalum@hms.harvard.edu, call 617-384-8520 to leave a voice message, or write us at Rounds, Alumni Affairs and Development, Harvard Medical School, 401 Park Drive, Boston, MA 02215. Please include your name and class year. We may call you if we need to clarify information or verify that the story was indeed submitted by you. Stories also may be edited for length and clarity.

We welcome your feedback on this new effort. And we look forward to sharing your stories in coming issues of *Harvard Medicine*.

1964

Robert Reynolds

After relocating from Johns Hopkins, where I was an associate dean, to the University of Virginia as professor of medicine and senior associate vice-president for health sciences, I served as UVA vice-president and chief information officer. This switch from medical administration to university-wide IT was challenging and exciting.

I was called out of my first retirement to implement EPIC, the completely computerized hospital and clinical medical record system, for the UVA Med-

ical Center. I retired for a second time in 2010 and am thoroughly enjoying the freedom!

1993 25th REUNION

Robert Vonderheide

I've been named director of the Abramson Cancer Center of the University of Pennsylvania, where I will lead the efforts of more than 400 basic, translational, and clinical scientists working to advance new treatments and cures for cancers of all kinds. I'm proud to say that the Abramson Cancer Center has been ranked among the nation's most highly rated cancer centers by the National Cancer Institute.

At Penn, I also serve as the Hanna Wise Professor in Cancer Research, vice-chair for research in hematology-oncology, and co-director of the Parker Institute for Cancer Immunotherapy.

1998

Alfredo Quinones-Hinojosa

I am excited to announce that I was recently named the William J. and Charles H. Mayo Professor. I also serve as chair of the Department of Neurologic Surgery at the Mayo Clinic in Jacksonville, Florida.

OBITUARIES

REMEMBERING DISTINGUISHED LIVES

1940s

1940

Nathaniel B. Kurnick
February 18, 2017

1944

Neville K. Connolly
January 30, 2017

1945

Walter A. Wichern Jr.
March 27, 2017

1946

Armand L. Bengle Jr.
April 13, 2017

Wade N. Miller
May 6, 2017

1947

John W. Littlefield
April 20, 2017

1948

J. Jerrold Applegarth
May 8, 2017

1950s

1952

William S. Joyner
April 8, 2017

B. Perry Ottenberg
March 7, 2017

1953

Kenneth F. Anderson
February 1, 2017

1954

Richard C. Burnstine
February 21, 2017

1955

Norton I. Gettes
April 1, 2017

1956

Donavin A. Baumgartner Jr.
April 3, 2017

Robert S. Cotsen
February 11, 2017

John M. McRae Jr.
April 2, 2017

1957

Thomas L. Hall
May 20, 2017

1958

Ronald J. Messer
April 27, 2017

1959

Hall Downes
January 8, 2017

1960s

1961

Michael J. McKeown
January 26, 2017

1962

Eliot L. Berson
March 19, 2017

1963

Faith B. Davis
April 16, 2017

1964

Robert W. McCarley
May 27, 2017

David A. Ontjes
May 7, 2017

Joel M. Seidman
February 13, 2017

1965

Robert L. Kane
March 6, 2017

1967

Richard F. Kempczinski
March 8, 2017

1970s

1972

John F. Trowbridge
March 13, 2017

1975

Ulder J. Tillman
January 3, 2017

1980s

1980

Virginia T. Latham
April 21, 2017

1984

Louis M. Teresi
April 26, 2017

2000s

2009

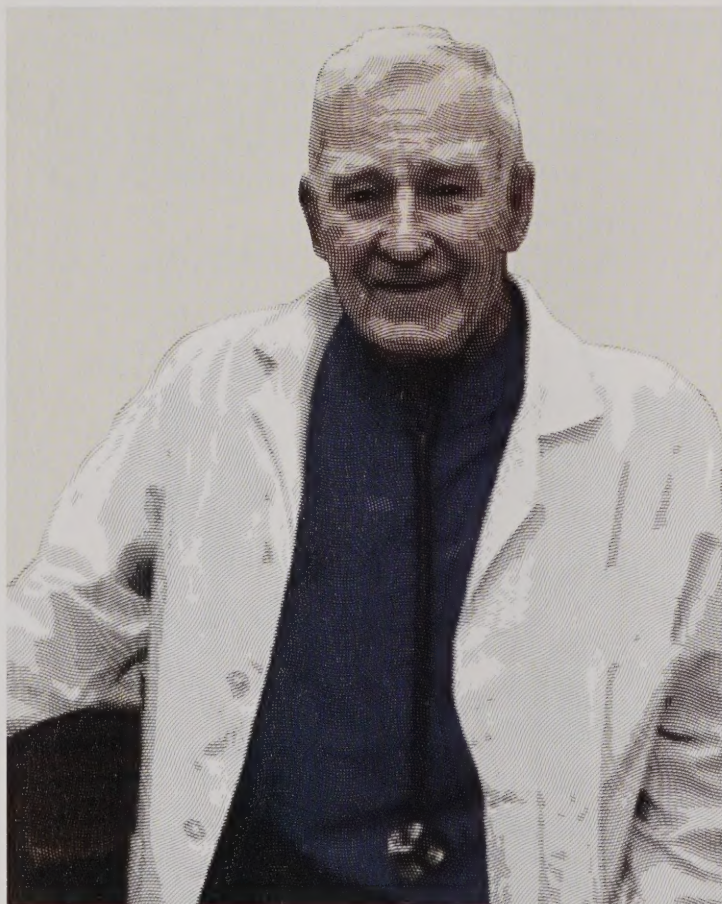
Ali R. Attarpour
May 25, 2017

This listing of deceased alumni includes those alumni whose notices of death were received between February 11 and June 2. A complete list of deceased alumni can be found at hms.harvard.edu/memoriam.

If you know of an HMS alumna/us who has died recently, please email hmsalum@hms.harvard.edu.

TAKING A HISTORY

PROFILE OF LLOYD HAMILTON, CLASS OF 1954



CLAIMS TO FAME

Director, Health Lifeline, Nyack, New York

DAISY CHAIN

Lloyd Hamilton grew up along the Delaware River in Lambertville, New Jersey. By the age of five, he knew he wanted to be a doctor. After all, his father, uncle, grandfather, and great uncle were all physicians.

"Everyone called me 'little doc,'" Hamilton says. Friends

would bring him their sick cats and dogs to diagnose and treat. "I was just naturally curious."

That curiosity and passion for medicine has not dimmed during the more than eight decades that have followed.

SHAPING A FUTURE

Following his high-school graduation, Hamilton began his World War II military service as a hospital corpsman for the U.S. Navy. After the war ended, he worked alongside an orthopedic surgeon at Camp Lejeune in North Carolina. "Happily for me," he says, "they kept me for an extra year because of my orthopedic-tech specialty training."

Next stop for Hamilton was Yale University, where he developed an interest in psychiatry that was sparked by his reading the works of Sigmund Freud.

TANDEM INTERESTS

Hamilton's inquisitive nature led him to pursue two medical specialties: psychiatry and internal medicine. He trained in psychiatry at the New York State Psychiatric Institute, part of Columbia University Medical Center, where he served as a hospital psychiatrist. In the 1960s, Hamilton was the clinical director of what was then known as Hillside Hospital, a psychiatric hospital in Queens.

In the late 1970s, Hamilton embarked on a second residency, in internal medicine, at Stamford Hospital in Connecticut. "I was active in psychoanalytic training and clinical work, which I always enjoyed," he says. After

that residency, he remained at Columbia but, between 1981 and 1998, also ran a private primary care practice in Nyack, New York, and worked at Nyack Hospital. In 1990, he retired from Columbia to work part time as a primary care physician in a clinic in Pomona, New York, run by the Rockland County Department of Health, for people who are without health insurance.

FULL SAIL SET

When the loss of funding forced the clinic to close in 2008, Hamilton was determined to find a way to continue serving a community that had depended on its services.

"The patients had nowhere to go," he says. In 2009, with support from a friend and a local church, Hamilton opened the Health Lifeline clinic in Nyack. The clinic is staffed by nurses, administrative staff, and one doctor—Hamilton—all of whom volunteer their time.

"My colleagues at the clinic still inspire me," he says. Despite the challenge of relying solely on donations for all their operating expenses, the clinic has remained open, caring for patients two days a week.

Hamilton and his wife now revisit the many journeys that have formed a special part of their marriage. Those journeys include the couple's four transatlantic crossings by sailboat. Their life together has also included Hamilton's journey back to the sort of community medicine practiced by his physician forebears so many years ago.

—Katie DuBoff



HARVARD
MEDICAL SCHOOL

"I work with the faculty,
students, staff, and researchers
at Harvard Medical School.
So it is a privilege to give to
an institution I know well."

— Lisa Mayer, EdM '81

Executive Director,

Giovanni Armenise-Harvard Foundation



WHAT WILL BE YOUR LEGACY?

Lisa Mayer has worked at HMS
for 17 years. Her deferred gift annuity
establishes a teaching and research
fund to support the HMS Family Van,
a mobile health clinic. She will receive
fixed income for life, with payments
postponed until she needs them.

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